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Yale medicine

autumn 2005

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**ON THE COVER**

A Marine rests during operations in Parwana, Iraq, in August. The Marines were seeking insurgents in the western Iraqi town just days after a roadside bomb killed 14 of their comrades.

BACKGROUND

Soldiers guard the scene of an attack on an armored personnel carrier, still blazing in the distance, in West Baghdad in April.

AP/Wide World Photos

On the Web

yalemedicine.yale.edu

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AUTUMN 2005

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As long as humans have waged war, the horrors of the battlefield have caused psychological damage. As troops return from Iraq, therapists, psychiatrists and veterans of previous wars are helping them return to civilian life.

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Working in a Yale laboratory in the 1940s, Dorothy Horstmann solved a puzzle that would lead to the first polio vaccine.

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Article ignored ethical aspects of stem cell research

I was disappointed with the *Chronicle* piece by Marc Wortman ["For Stem Cell Researcher, Connecticut's Initiative Offers a New Avenue for Progress," Summer 2005] that involved an interview with Diane Krause, M.D., PH.D., and focused on her support for human embryonic stem cell research.

The superficial approach of the article minimized the ethical controversies of human embryonic stem cell research and offered readers an unbalanced and misleading feel-good article.

Lacking was acknowledgment that, with the technology currently available, human embryonic stem cell research involves the destruction of human embryos. As a former human embryo myself writing to another former human embryo (yourself), it should not need to be stated that human beings

come from human embryos, but advocates of human embryonic stem cell research seem unwilling to acknowledge this basic biological fact. I was particularly chilled by Dr. Krause's statement that she wants "the freedom to use embryonic stem cells as a tool." I think the piece should have noted that there exist some serious and complicated moral and ethical concerns in this type of research even if Dr. Krause is seemingly not troubled by them.

If anything, Dr. Krause's own work with adult stem cells suggests that we have much to gain from that line of research, which does not have the same moral and ethical difficulties as research with human embryonic stem cells. The article failed to mention that to date thousands of living patients have been helped with adult stem cell technology. This includes patients with spinal cord injuries, genetic and metabolic disorders, impaired heart function and so on. It did not mention that no one has yet been helped in any way by embryonic stem cells.

I would like to have seen a better analysis of these grave and pressing issues in your magazine. I hope *Yale Medicine* will take on this controversial topic in a more comprehensive manner with a future feature article.

Robert Kaladish, M.D.
Amherst, N.H.

Article on schistosomiasis was inspiring

I want to congratulate Kohar Jones for her impressive and beautiful article ["The Silent Scourge of Development," Summer 2005], and you, for publishing it. Especially in this period when greed and deception are often so dominant, to see something like that article is particularly inspiring and a reminder that there are wonderful people in this world, young as well as old. Please pass my comments on to her. She deserves any recognition she gets.

John Strauss, M.D.
Professor emeritus of psychiatry
New Haven

Ibn Sina's roots

I enjoy reading the articles in *Yale Medicine* very much and I think the magazine offers an excellent selection of topics.

Just as a quick note, in the mustard gas article ["From the Field of Battle, an Early Strike at Cancer," Summer 2005], you refer to Ibn Sina, the 10th-century physician and scholar. He was actually Persian, not Arab. The reason he wrote in Arabic was that the official language for science in Iran was Arabic after the Arabs conquered the Persian Empire.

Thanks again for the excellent ideas and articles!

Setareh Vistamehr, M.D.
Instructor, Department of
Ophthalmology and Visual Science
New Haven

As Dr. Vistamehr notes, Ibn Sina, known as Avicenna in Europe, was not an Arab. Because he was born in what is now Uzbekistan and died in what is now Iran, his roots are a subject of debate. For more on Avicenna, see "From the Middle East, in the Middle Ages," p. 16, in this issue. —Eds.

Have an opinion? Write to us at ymm@yale.edu

HOW TO REACH US

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Nostalgia of another kind

In 1980, years after the last troops returned home from Vietnam, the military and medical establishments put a name on the psychiatric sequelae that have afflicted soldiers for as long as there has been war—post-traumatic stress disorder (PTSD). Documented since the time of Homer and variously known as nostalgia, combat fatigue and shell shock, it is marked by anxiety, flashbacks, irritability and withdrawal from society, among other symptoms. In our cover story we examine PTSD and its implications for troops coming home from Iraq. To find out what has been learned about PTSD and how the experience of Vietnam veterans is helping today's troops, writer Cathy Shufro spoke with Vietnam and Iraq veterans as well as psychiatrists and social workers at Yale and the Connecticut Healthcare System in West Haven.

We also look back half a century to the days when parents kept children away from public pools and beaches in the summertime. Polio was a dread disease, but scientists were getting closer to discerning how it acted and how to prevent it. Among those scientists was the late Dorothy M. Horstmann, M.D., FW '43, a member of the Yale Poliomyelitis Study Unit, who made a key discovery about polio

antibodies that paved the way for development of vaccines. We asked David M. Oshinsky, PH.D., a historian at the University of Texas at Austin, and author of *Polio, An American Story*, to profile the first woman to become a professor of medicine at Yale.

Finally, in this issue we profile Robert J. Alpern, M.D., who took over as dean almost a year and a half ago. As *Yale Medicine's* editor, Michael Fitzsosa, reports, Alpern has spent the time assembling his management team, getting to know the medical school and launching a strategic plan to move the school forward.

John Curtis
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SECOND OPINION BY SIDNEY HARRIS



"... AND IF YOUR SYMPTOMS DISAPPEAR WITHIN THREE DAYS, I'LL GET A LARGE GRANT."

A mouse offers a new way to test vaccines

By implanting a human immune system into mice, scientists plan to study vaccines.

The laboratory mouse—resilient, easy to breed and ideally suited to the genetic manipulations that form the basis of much of modern biomedical research—has been invaluable to immunologists such as Richard A. Flavell, PH.D., chair and Sterling Professor of Immunobiology. But there are limits to the usefulness of this most versatile of research animals in immunology, because the mouse immune system has been tailored over evolutionary time to deal with pathogens different from those that infect humans. To compensate, scientists like Flavell supplement their work in mice with studies of human immune cells in culture, but here, too, there are inherent compromises. The immune system, a multifaceted mechanism distributed throughout the body, is difficult

to emulate in a petri dish, and the behavior of cells in culture can be a poor predictor of how a drug will work in the living human body.

Since ethical considerations prohibit testing drugs in humans before they've been proven safe and effective, these intrinsic limitations of the tools available to immunologists mean that bringing vaccines and other cures from the laboratory to the clinic often requires a leap across an unavoidable knowledge gap.

"You don't really want to be studying mouse cells; you want to study human cells, and ultimately you study humans in clinical trials," said Flavell, who is also a Howard Hughes Medical Institute investigator. "There are enormous difficulties making sure that what you do in clinical trials is safe and isn't going to adversely affect the patient."

But a remarkable advance in a Swiss laboratory may provide a long-sought bridge between the bench and the bedside for immunologists. In 2004, Markus G. Manz, M.D., and

colleagues at the Institute for Research in Biomedicine created a rudimentary human immune system in mice by injecting human umbilical-cord blood containing stem cells and other progenitor cells into a mutant strain of mice that lack immune systems.

Manz's paper appeared just as the Grand Challenges in Global Health initiative was accepting final proposals for grants. The initiative, funded by the Bill & Melinda Gates Foundation, the Canadian Institutes of Health Research and the Wellcome Trust, and administered by the Gates Foundation, planned to distribute more than \$436 million to support innovative research on diseases that afflict the world's poorest people. Flavell proposed that his team join forces with Manz and with Tarrytown, N.Y.-based biotech company Regeneron Pharmaceuticals to perfect a mouse model of human immunity for testing vaccines. In late June, Flavell learned that the initiative would award \$17 million to the project.

"It's akin to a 'Manhattan Project,' to make this work like a true human immune system, so you could really do experimentation that is predictive of the human response," Flavell said.

A mouse model of human immunity, for example, would allow scientists to test a vaccine for HIV, which has heretofore been impossible because mice are normally not susceptible to the virus. But Flavell said that the technique will have any number of applications. "This system, once it's up and running, could be used to study all kinds of things," he said.

Elizabeth E. Eynon, PH.D., a research scientist in Flavell's lab, said that the model could make clinical trials much more efficient. "The FDA will require people to do just as many Phase I and Phase II trials as they do now," she said, "but the likelihood of failure at those stages would be reduced if we can show safety and efficacy beforehand."

—Peter Farley



Marna Borgstrom named to head Yale-New Haven Hospital and Health System

Since she joined Yale-New Haven Hospital (YNHH) as a junior administrator in 1979, Marna P. Borgstrom, M.P.H. '79, has become a vice president, the chief operating officer and, as of October 1, the CEO and president of the hospital and the Yale New Haven Health System (YNHHS). She succeeds Joseph A. Zaccagnino, M.P.H. '70, who retired on September 30 after a 35-year career at the hospital.

During more than a quarter-century at the hospital she has watched it grow into the 944-bed flagship of a health system that stretches along Long Island Sound from Rye, N.Y., to Westerly, R.I. It is the hub of a New Haven health care delivery network that includes a children's hospital, a psychiatric hospital, two independent ambulatory surgical centers, a large radiology practice and the Shoreline Medical Center in Guilford.

Working with Zaccagnino, Borgstrom oversaw the hospital's \$850 million budget and served as the primary liaison to the School of Medicine. She led the planning and construction of the children's hospital, and headed up a patient safety program that trained 40 senior managers under General Electric's process-improvement initiative known as Six Sigma. As the second-in-command at the hospital for more than a decade, Borgstrom helped develop YNHHS, an affiliation of several dozen organizations including YNHH and two other large hospitals, in Bridgeport and Greenwich, that encompasses their networks of physi-

cian practices, surgical centers, diagnostic facilities, rehabilitation centers, pharmacies and visiting nurses.

"We want to be the provider of choice—locally, of course, but also regionally and nationally," she said. The hospital's regional and national distinction, which Borgstrom intends to build on, reflects joint investments in unique clinical programs with the School of Medicine. She is looking forward to the construction of a \$440 million clinical cancer center, currently awaiting approval from New Haven zoning officials, that will provide needed capacity for current and emerging clinical initiatives.

Other recent achievements of YNHHS include the creation of an emergency angioplasty program at Greenwich Hospital in collaboration with YNHH and physicians at the School of Medicine. Previously, emergency patients in Greenwich had to be transported out of town for the procedure. Now they can be treated locally, and elective angioplasty cases and cardiac surgeries will be referred from Greenwich to New Haven.

A revamped liver transplantation program that began operations in July has the potential to draw pediatric patients from the region and beyond, and many joint programs—in epilepsy, endocrine surgery and maternal-fetal medicine, to name several—already bring patients to New Haven from across the country. Borgstrom would like to see the list grow, so that more out-of-state patients come to the city for care.

Her appointment came a little more than a year after the arrival of medical school Dean Robert J. Alpern, M.D., in



Marna Borgstrom became the head of the Yale-New Haven Hospital and the Yale New Haven Health System on October 1.

June 2004. Based on her work with Alpern during his first year here, Borgstrom sees "unprecedented opportunities" ahead for the hospital and medical school. Alpern called Borgstrom "an excellent choice for the job of CEO."

Borgstrom earned her public health degree in hospital administration at Yale in 1979. She said the program gave her a footing in how to analyze and solve problems at a large health care organization, and also an appreciation for the public health challenges facing health care executives.

—Michael Fitzsosa



Artist Laura Ferguson uses medical images in her Visible Skeleton Series, which was displayed at the National Museum of Health and Medicine in Washington in the spring of 2005. This work from the series incorporates oils, bronze powder, charcoal, colored pencil, pastel and oil crayon on paper.

Portraits in light— artists blend medical imagery into their work

In the 1990s, when Bettyann H. Kevles, M.A., asked listeners of the National Public Radio program *Science Friday* to imagine their bodies intertwined with medical technology, she received seven responses, all from artists. All seven had experienced imaging techniques such as X-rays, magnetic resonance imaging, computed tomography (CT) scans and other routine procedures. One described them as “portraits in light.”

A lecturer in Yale’s Program in the History of Medicine and Science, Kevles studies how new technologies become a part of everyday life. But having grown up in a family of painters and having studied painting herself, Kevles has a long-standing interest in art. Over the years, she has built up a library of work by visual artists who explore their medical conditions in their paintings. She explored this theme, in part, in her 1997 book, *Naked to the Bone: Medical Imaging in the 20th Century*, and in *Picturing DNA*, written with Marilyn Nissenson and published online in 2000.

At a symposium on brain imaging at the annual meeting of the American Association for the Advancement of Science in Washington in February, Kevles presented the work of visual artists who had used medical imaging to create self-portraits. The survey reached back to the early 20th century and the work of Mexican painter Frida Kahlo, whose spine was severely injured in an accident when she was an 18-year-old student, and whose self-portraits

show her body and spine from the inside in a manner reminiscent of X-rays. Many contemporary artists have incorporated more modern techniques. New York artist Laura Ferguson, who suffers from scoliosis, studied anatomy, consulted with orthopaedic surgeons and radiologists and imaged her body with a 3D spiral CT scan, which allowed her to visually manipulate her skeleton to observe it from different angles and in different postures. Her *Visible Skeleton Series*, a visual autobiography created by blending many layers of colors on paper, was on display at the National Museum of Health and Medicine in Washington this spring.

Since writing her 1997 book, Kevles has continued her study of artists such as Jennifer Hall of Boston, who has temporal lobe epilepsy and used an electroencephalogram to capture her brain waves during a seizure. She then used a computer program to transform the erratic spikes into a three-dimensional image and cast it in silver in the shape of a tiara.

In her more recent work, Kevles has explored the idea that turning medical imaging techniques into tools of self-exploration allows artists to work through their illness so they can get past seeing themselves as victims of it. “Having seen whatever it is—plaques in their brain, or an EEG of a crazy electrical storm—they no longer think of themselves as epileptics, for example. They’re people with particular parts of their bodies that don’t work,” Kevles said. “Many artists feel that their art, in this way, gives them power over their conditions.”

—Alla Katsnelson



MICHAEL MASSLAND

GREY NAMED DEAN OF NURSING

Margaret Grey, R.N., DR.P.H., was named dean of the School of Nursing in July. Grey, previously associate dean for scholarly affairs, joined the faculty in 1993. She succeeds Catherine L. Gilliss, D.N.Sc., who served as dean from 1998 until last year. Grey, an internationally known researcher in the natural history of adaptation to chronic illness in childhood, is the author of more than 160 publications.

Yale endowment earns 22 percent, as investment steward earns plaudits

News of outstanding returns on Yale's endowment came as the university's chief investment officer was already riding a wave of favorable publicity. David F. Swensen, PH.D. '80, had recently published his book *Unconventional Success: A Fundamental Approach to Personal Investment* (Free Press), and finance journalists were calling him the best money manager in academia. They pointed to Swensen's track record as manager of Yale's endowment over the past 20 years, which has seen average returns of 16 percent. For the 2004 fiscal year, the endowment earned returns of 22.3 percent, bringing total assets to \$15.6 billion. And under Swensen's leadership, the Yale endowment routinely outperforms Standard & Poor's 500. He credits his success to a nontraditional asset allocation with an emphasis on equity investments.

In numerous interviews with the press, however, Swensen cautioned that

individual investors are unlikely to reap his returns, even if they read his book. Those who spend a few hours a week on their portfolios simply can't compete with institutions such as Yale that have a team of full-time professionals actively managing the endowment.

"The outstanding performance by the investments office in the past year has matched a record of achievement over time that has earned David Swensen and his colleagues the highest possible praise and admiration from their peers," President Richard C. Levin said in a press release. "Yale's capacity to fulfill its ambitious mission has been greatly enhanced by their superb stewardship of the endowment."

Because of Swensen's efforts, the endowment's share of the university's operating budget has more than doubled over the past decade. The endowment now contributes almost a third of the university's revenues—\$610 million this fiscal year—the largest single source of support.

—John Curtis

et cetera ...

GOLDMAN-RAKIC FELLOW NAMED

Susheel Vijayraghavan, a graduate student in neurobiology at the School of Medicine, has been selected as the recipient of the 2005 Patricia S. Goldman-Rakic Fellowship. This fellowship, established by Yale and the pharmaceutical maker Pfizer in 2003, honors the memory of the late Yale professor Patricia Goldman-Rakic, PH.D., and highlights excellence in neuroscience research at the medical school. According to Lynn Cooley, PH.D., director of the Combined Program in the Biological and Biomedical Sciences, Vijayraghavan's selection is a "tribute to Dr. Goldman-Rakic's distinguished career and to Susheel's developing career."

Vijayraghavan studies the effects of dopamine on working memory in primates and was Goldman-Rakic's final graduate student before her death in 2003. As the fellowship recipient, he will receive tuition, a stipend and health care coverage, as well as additional funds for travel to scientific meetings.

—J.C.

YALE WEBSITE DESIGNERS HONORED

Patrick J. Lynch, M.S., director of the Med-Media Group of Yale's Information Technology Services, and C. Carl Jaffe, M.D., professor of medicine (cardiology), received the 2005 Pirelli Prize for Multimedia Education and the Top Pirelli Prize for 2005 for the educational website "Introduction to Cardiothoracic Imaging." The prizes, which they received in Rome in June, honor technical innovations and contributions to science education through the outstanding communication of science and technology.

The Pirelli S.p.A. Group, one of Europe's major telecommunications and manufacturing firms, has underwritten the awards since their inception in 1996. The Pirelli jury cited the extraordinary depth and breadth of the cardiothoracic imaging site (<http://info.med.yale.edu/intmed/cardio/imaging>).

"At no time in history does the intersection of media and science education matter more," said Jaffe, who retired in July after 35 years on the faculty of the School of Medicine. "Ignorance of or, more importantly, denial of the truths of science obscures recognition of our common humanity."

—J.C.



JIM FRAZIER

Biomarkers warn of a “silent killer”

High or low levels of certain proteins can signal the likelihood of ovarian cancer.

Epithelial ovarian cancer ranks as the most lethal of gynecological malignancies. It is only 10 percent as common as breast cancer, but its mortality rate is three times as high. The reason is simple: routine mammography and breast examinations can catch breast cancer early, but no such screening exists for ovarian cancer in its early stages. With few early symptoms, the disease passes under the medical radar until it has reached later stages of malignancy, and therapeutic options are often limited.

Now a group headed by Gil Mor, M.D., PH.D., associate professor of obstetrics, gynecology and reproductive sciences, has found a way to detect the “silent killer” in its earliest stages, according to a report in May in the *Proceedings of the National Academy of Sciences*. The researchers at Yale, George Washington University and the Nevada Cancer Institute devised a still-unapproved screening test that measures levels of four cancer-related proteins—leptin, prolactin, osteopontin and insulin-like growth factor II (IGF-II)—in blood samples. These biomarkers are proteins that change in response to several different forms of cancer, perhaps as part of the immune response. “Our strategy is unique in that we are using a combination of proteins representative of how the total system reacts to cancer, rather than focusing on one protein,” said Mor.

Previous studies had identified each of the four proteins as possible biomarkers, but Mor’s team found that individually none of the proteins served as a reliable indicator of cancer.

The researchers began with 169 proteins linked to epithelial ovarian cancer. They then narrowed the list to 35 proteins that were either far more or far less prevalent in women with advanced cancer than in healthy women. They further refined the biomarker pool to the four proteins, two of which are consistently overproduced (prolactin and osteopontin) and consistently underproduced (leptin and IGF-II) in women with cancer.

To put these findings to clinical use, women need only have blood drawn. Levels outside of the normal range of two or more of the biomarkers predict cancer. Follow-up analyses, such as ultrasound, can verify the diagnosis.

In a preliminary study of more than 200 women, the screen accurately detected ovarian cancer in 95 percent of cases. The specificity of the test—those correctly diagnosed as disease-free—also stood at 95 percent, but Mor stressed that the test is not ready for screening the general population. “Because this disease is relatively rare, a specificity of 95 percent means that 5,000 out of every 100,000 women tested by this method would give a false-positive result. That’s not acceptable,” he said. To increase the screen’s specificity to an acceptable 99.6 percent, Mor’s team is looking at adding three more proteins to the biomarker pool.

—Kara Nyberg

et cetera...

With the Canary Database, animals become sentinels for environmental hazards

Before the effects of mercury poisoning showed up in the children of Minamata, Japan, in the 1950s, cats were getting sick with a neurological ailment dubbed "dancing cat disease." In Africa, human outbreaks of the lethal Ebola virus follow the dying off of animals including apes and deer. And epidemiologists are keeping a watchful eye on avian flu, which has jumped from chickens to humans in Asia and Europe.

Since 2002 an interdisciplinary group of researchers at Yale has been creating a database that makes the connections between diseases in animals and diseases in humans. With funding from the National Library of Medicine, the Canary Database hopes to harness this information so that animals can serve as sentinels of impending human disease.

"If you have an animal that is sick from an environmental hazard, should human health professionals be concerned?" asked Peter M. Rabinowitz, M.D., M.P.H. '95, FW '98, associate professor of medicine and principal investigator of the database. The question is not hypothetical. It was a veterinarian at the Bronx Zoo who in 1999 reported the occurrence of dead crows to public health authorities, who did not initially recognize that the birds were signaling the emergence of West Nile virus in this hemisphere. "That is a good example," Rabinowitz said, "of the communication barrier and world-view barrier we are trying to bridge."

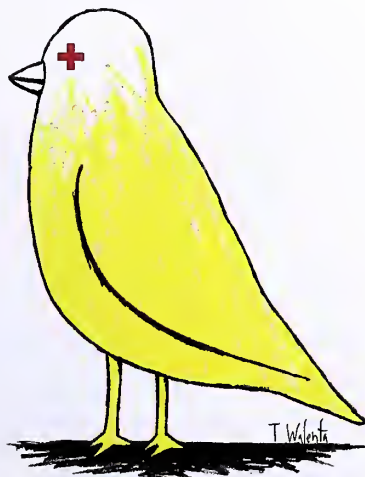
In order to overcome gaps between experts in animal health and those in

human health, the Canary Database makes animal sentinel studies from a variety of biomedical databases easily accessible. Researchers can search the database for a wide variety of environmental hazards, both toxic and infectious; learn how these hazards have been studied in animal populations; and discover whether there is evidence linking the animal disease event to human health risk.

The database takes its name from the proverbial canary used by coal miners to warn of the presence of carbon monoxide. A collaboration of the Yale Occupational and Environmental Medicine program, the Yale Center for Medical Informatics and the U.S. Geological Survey National Wildlife Health Center, the database culls from veterinary literature papers on animal disease that might have relevance to humans. Five curators, including veterinarians and physicians around the country, review and curate the papers, adding information about epidemiological methods and linkages to human health outcomes.

The information they collect could be used to help public health practitioners detect impending disease outbreaks or terror attacks involving chemical or biological weapons. "We want to be a continuing resource," Rabinowitz said.

—John Curtis



ALCOHOL LOWERS CANCER RISK

The incidence of non-Hodgkin's lymphoma (NHL) is rising throughout the world—in industrialized nations it ranks as the sixth most common cancer among men and the eighth most common among women. Although studies have suggested that alcohol consumption may lower the risk of NHL, results have been inconsistent.

In July a team at the Department of Epidemiology and Public Health reported in the journal *Lancet Oncology* that alcohol consumption does indeed lower the risk of NHL. Unlike prior studies, this one pooled data from nine studies covering more than 15,000 people in the United States, the United Kingdom, Sweden and Italy. "This study with a large sample size allows us sufficient statistical power to analyze the data by type of alcohol consumed and disease subtype," said principal investigator Tongzhang Zheng, Sc.D., professor of epidemiology.

Further studies are needed to explore the link between alcohol consumption and the lower risk of NHL.

—J.C.

MUSIC AND SEDATIVES

For decades, doctors and nurses in the operating room have turned to music to soothe the nerves of anxious patients. Several studies have found that patients who listen to music are less anxious before surgery and need less anesthesia.

But Zeev N. Kain, M.D., HS '92, FW '93, professor of anesthesiology, pediatrics and child psychiatry, wondered whether music did more than simply drown out the racket in the operating room. With colleagues at Yale and the American University of Beirut in Lebanon, he designed a study in which patients who had received spinal anesthesia—but were awake—could control the dosage of a sedative. They listened through headphones to either music of their choice or white noise generated by a relaxation device. As reported in May in the journal *Anesthesia and Analgesia*, patients who listened to music used significantly less sedative.

"Doctors and patients should both note that music can be used to supplement sedation in the operating room," Kain said.

—Peter Farley

A moth's gene helps discern gene functions

A piece of DNA from a moth could signal a major leap in the understanding of what specific genes do.

A new tool for genome research, developed in the Yale laboratory of Tian Xu, PH.D. '90, professor and vice chair of genetics, professor of molecular oncology and development and a Howard Hughes Medical Institute investigator, promises to greatly accelerate the work of assigning purpose to thousands of unexplored human genes.

The tool is a jumping gene, a small piece of DNA called a transposon that moves around the genome, usually settling in other genes and allowing scientists to suppress the activity of existing genes or insert new ones.

Transposons are active in many plant and insect genomes and have helped to make the fruit fly *Drosophila* the darling of geneticists, as these mobile DNA fragments were used to decipher the role of nearly every gene in that model organism. But for decades scientists

could not find an equivalent transposon for mammals.

As reported in the August 12 issue of the journal *Cell*, Xu and his colleagues manipulated a transposon called *piggyBac*, found in the cabbage looper moth, so that it can be easily cut and pasted into the genomes of higher organisms, including mice and humans. "With this transposon, we now have the ability to systematically inactivate each and every gene in a model organism like the mouse," Xu said.

In mouse studies, scientists have traditionally used chemicals to modify genes, but this approach is painstakingly slow, and it can be difficult to locate the genes that have been mutated. The *piggyBac* transposon, when injected into fertilized mouse eggs along with an enzyme called transposase, is remarkably efficient at inserting itself into important coding regions of the genome, and as its name implies, it carries genetic tags that allow researchers to locate mutations quickly.

Moreover, *piggyBac* has the added feature of total reversibility, which should allow scientists to verify that particular mutations have particular effects. In the presence of transposase, *piggyBac* easily hops into genes, and it remains in place in any offspring in subsequent generations that do not inherit the enzyme. But when these mice are mated with others who carry the transposase gene, *piggyBac* hops back out of genes without leaving a trace.

These traits make *piggyBac* a "dream tool" for geneticists, Xu said. "This new technology will completely change the game of using mutagenesis to understand the function of mouse genes and, by extension, their human counterparts." *PiggyBac* could also be a promising new vehicle for human gene therapy, according to Xu, who said that, in addition to carrying tags, *piggyBac* can be engineered to carry new genes into the genome.

To demonstrate the potential of this genetic piggybacking, Xu and his colleagues used *piggyBac* to insert a gene for a protein that glows red under ultraviolet light into a mouse. However, many more experiments will be required to determine whether the transposon, or some variation of it, could reliably and safely transfer therapeutic genes to humans.

Xu's immediate goal is to use *piggyBac* to inactivate every gene in the mouse, one by one, a project that would be unthinkable with traditional mutagenesis methods. "For the past two decades, it has routinely taken about a year to mutate one gene in a mouse, and altogether about 3,000 genes have been knocked out in mice, out of a total of about 25,000 that are in the genome," Xu explained. With the help of *piggyBac*, he said, "in three months, with two students, we have done 75 genes."

—Pat McCaffrey



GERO MIESENBOCK

USING LASERS TO DETERMINE CELL FUNCTION

Through genetic tweaking, researchers at the School of Medicine have made fruit flies walk, jump and fly on command—by flashing a light at them. The scientists inserted rat ion channels into nerve cells that control flies' escape movements, then injected the flies with a chemical that would activate the ion channels when exposed to light. Gero A. Miesenböck, M.D., associate professor of cell biology at the medical school, who led the study that appeared in the journal *Cell* in April, said that the research offers a new way to learn how nerve cells govern behavior.

A livestock virus may offer a new approach to treating glioblastoma

Viruses are hijackers, wreaking infectious havoc by taking over a cell's machinery and using it to replicate. But their wily ways may not be all bad. Yale professor of neurosurgery Anthony van den Pol, PH.D., is harnessing their destructive power to develop a novel treatment for glioblastoma, the most common and aggressive form of brain cancer.

Glioblastoma strikes about 7,000 Americans each year, and most patients live just a year after diagnosis. Although it can be treated with surgery, radiation and chemotherapy, said van den Pol, the cancer usually comes back.

The idea of unleashing viruses to destroy tumor cells is beginning to gain validity, not just for brain cancers but also for ovarian, prostate and other kinds of tumors. When this line of research began two decades ago, scientists feared that the viruses would spread to healthy cells, so they genetically altered them to prevent them from replicating. But

those inactivated viruses kill relatively few brain tumor cells. The Yale team hypothesized that a replicating virus would be much more effective.

Van den Pol and his colleagues bred several generations of vesicular stomatitis virus on glioblastoma cells, selecting for strains with the highest tumor-killing capacity. Then they tested the virus and saved those strains that did not infect normal cells. In a study published in the *Journal of Virology* in May, the researchers reported that the strain they developed selectively killed glioblastoma cells *in vitro*, and was able to infect and kill whole tumors in mice.

The results are promising, but van den Pol stressed that they are still preliminary. The team plans to expose the virus to different types of cells found in the brain to make sure that it will not infect them. "This is a high-risk strategy," he said, "but we're dealing with a disease for which at present there is no cure."

—Alla Katsnelson



NEW TARGET FOR MELANOMA

Using a technology devised at Yale five years ago, researchers have found what may be a new target for treatment of melanoma. The Yale team used AQUA (automated quantitative analysis) to measure protein expression in melanoma tissue microarrays. In a study in *Nature* in July they reported that microphthalmia-associated transcription factor (MITF), a protein involved in cell survival, abnormally copies itself many times over. This overexpression was prevalent in metastatic disease and correlated with decreased rates of patient survival.

This suggests, said David L. Rimm, M.D., PH.D., HS '93, an author of the study and associate professor in the Department of Pathology, that MITF may represent a distinct class of oncogene that is necessary for tumor progression. Reduction of MITF activity sensitizes melanoma cells to chemotherapeutic agents, and targeting MITF in combination with other drugs may offer a new approach to treating melanoma.

—John Curtis

A TOLL ON INFECTIONS

In 1997 the late Charles A. Janeway Jr., M.D., and Ruslan M. Medzhitov, PH.D., professor of immunobiology, discovered toll-like receptors, or TLRs, molecules that alert the body's acquired immune system to the presence of microbial or viral invaders.

Scientists have since identified over a dozen types of TLRs, which detect proteins in bacteria and viruses but not those in the eukaryotic cells that make up our bodies. Some pathogens, however, are also eukaryotes, and a team at Yale and the National Institutes of Health wondered whether TLRs could recognize them.

In the June 10 issue of the journal *Science*, the group reported that TLR11, discovered in mice at Yale last year, triggers an immune response after it detects a protein in the virus that causes toxoplasmosis.

Team member Sankar Ghosh, PH.D., professor of immunobiology, said that while it is not yet clear whether humans have a functional version of TLR11, these studies should lead to development of novel strategies to combat these infections.

—Peter Farley



Cardiologist Harlan Krumholz has published a handbook that he hopes will encourage patients to be involved in their treatment for heart disease.

Guiding patients through heart disease

A cardiologist provides a handbook so patients can better understand their disease and how to treat it.

Half of all patients don't take the medications that their doctors prescribe. And the majority of cardiac patients leaving the hospital don't know the target numbers for optimal blood pressure or cholesterol. For cardiologist Harlan M. Krumholz, M.D., M.Sc., the Harold J. Hines Jr. Professor of Internal Medicine and of Epidemiology and Public Health, these findings reflect lost opportunities for patients to participate in their care. Hopes of fostering better patient involvement in their care motivated Krumholz to write *The Expert Guide to Beating Heart Disease: What You Absolutely Must Know* (HarperResource, \$14.95).

Krumholz said that patients who understand their disease and the options for treating it can collaborate more effectively with their physicians in choosing and following the strategies that are most likely to help them reach their goals. "If patients understand the rationale behind the strategies, they're more likely to follow them." Krumholz also argued that informed patients are more likely to get good care.

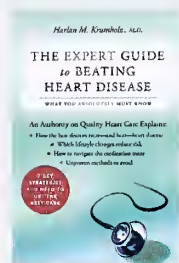
"We have this illusion that medicine is being practiced uniformly and is of high quality throughout the country," he said. "That perception is just not true. There is ample evidence that treatment strategies that are well-established by the literature and endorsed by national guidelines are not uniformly being recommended by doctors or pursued by patients."

Unfortunately, patients are not often encouraged to become well-educated about their condition, said Krumholz. "We're still in an era when most people come in, they're told what to do and given a prescription, and if they don't comply, they're seen as letting down the physician."

Patients seeking to educate themselves about heart disease may feel overwhelmed, however. "If you got sick, where would you start? There's such an avalanche of information," said Krumholz. He views his 152-page book as a "travel guide" that provides essential facts about how heart disease develops and what can be done to treat it. The book describes seven key strategies: controlling blood pressure, managing cholesterol, exercising, maintaining a healthy weight, managing blood sugar, quitting smoking and using medication effectively.

TERRY DAGRADI

For more on the book, visit
www.expertheartguide.com



Krumholz chose these seven strategies based on national guidelines and his expertise in evaluating the quality of heart disease care. A prolific researcher himself, he has helped set national standards for cardiovascular care for organizations ranging from the American College of Cardiology to the Department of Defense. Based on the published evidence, his book describes approaches that work (such as taking beta-blockers after a heart attack or controlling cholesterol with statins), those that probably help (eating fish regularly), those of uncertain value (taking vitamins) and those that have proven harmful (hormone replacement therapy for women).

A grant from the John A. Hartford Foundation in New York allowed Krumholz to hire a researcher—Susan Cheng, M.D., then a medical student at McMaster University in Ontario, now a resident in internal medicine at Johns Hopkins. Krumholz and Cheng field-tested the book: they sent about 100 copies to relatives, friends, friends of friends with heart disease and patients, asking them to circle sections that were confusing and to pencil in questions.

"We said, 'Write all over this. It won't hurt our feelings.'" Their approach seems to have worked; a critic for *Kirkus Reviews* writes that "Dr. Krumholz has a gift for translating jargon into clear, accessible language that the concerned reader can easily absorb."

Writing for a general audience was a departure for Krumholz. He has clinical responsibilities one day each week, and as director of the Robert Wood Johnson Clinical Scholars Program at Yale, he spends a lot of his time guiding postdoctoral fellows in the program as they do research on improving clinical care and population health. His own research appears in 40 to 50 articles annually. But he called those papers "just a means to an end."

"At the end of the day, it's not about the number of publications but about whether people can benefit from the work we've done. The book is a tool to help promote that."

—Cathy Shufro

Bookshelf is a column focusing on matters related to books and authors at the School of Medicine. Send ideas to Cathy Shufro at cathy.shufro@yale.edu.



Nanoscale Technology in Biological Systems

by Ralph S. Greco, M.D. '68, HS '73, et al. (CRC Press)

This book presents the latest information on the interface between nanotechnology and biology, examining the principles underlying the application of nanotechnology to basic science research, applied research and clinical practice.

Songs From the Black Chair: A Memoir of Mental Interiors

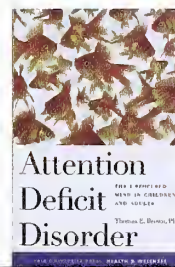
by Charles Barber, M.H.A., associate of the Yale Program for Recovery and Community Health (University of Nebraska Press) In his account of working with homeless mentally ill patients in New York, Barber tells their tales of prison, AIDS, heroin, crack and sexual abuse and of the voices that plague them.

The Craft of Psychodynamic Psychotherapy

by Angelica Kaner, PH.D., assistant clinical professor in psychiatry, and Ernst Prelinger, PH.D., clinical professor of psychology and psychiatry (Jason Aronson) Clinical vignettes illustrate the fundamentals of psychodynamic theory and technique, tackling questions such as: What is psychotherapy? How long will it take? How does change happen?

Information Systems Research: Relevant Theory and Informed Practice

edited by Bonnie Kaplan, PH.D., lecturer in anesthesiology (medical informatics), et al. (Springer) This volume is organized in seven sections, with 33 full research papers providing reviews on the Information Systems (IS) discipline. It also



includes papers featuring critical interpretive studies, action research, theoretical perspectives on IS research and the methods and politics of IS development.

Attention Deficit Disorder: The Unfocused Mind in Children and Adults

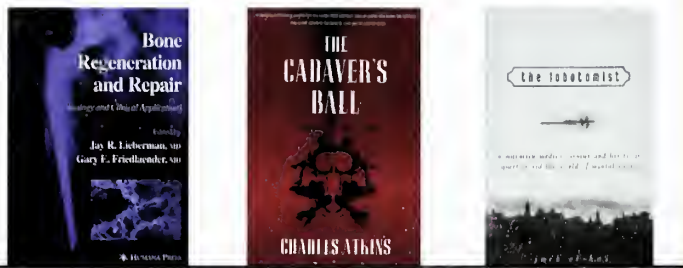
by Thomas E. Brown, PH.D., assistant clinical professor of psychiatry (Yale University Press) Drawing on recent findings in neuroscience and a variety of case histories from his own clinical practice, Brown defines Attention Deficit Disorder, describes how to recognize it in people of different ages and discusses how it can best be treated.

Heart Care for Life: How to Develop the Long-Term Personal Program That Works Best for You

by Barry L. Zaret, M.D., the Robert W. Berliner Professor of Medicine and professor of radiology, and Genell Subak-Sharpe, M.S. (Yale University Press) The authors outline the constants for the full range of cardiovascular conditions, from angina and heart attacks to high blood pressure and cardiac arrhythmias. They then guide readers through the process of assessing personal variables in order to develop an individual treatment and lifestyle program.

Emotional Comfort: The Gift of Your Inner Guide

by Judith M. Davis, M.D. '63 (Wilder Press) This book provides a self-hypnotic technique for attaining emotional comfort. According to Davis, the technique helps its practitioners to resolve chronic difficulties and to handle new ones that may arise.



Multiple Sclerosis as a Neuronal Disease

by Stephen G. Waxman, PH.D., M.D., professor of neurology, pharmacology and neurobiology (Elsevier Academic Press) This illustrated book brings together the latest information from clinical, pathological, imaging, molecular and pharmacological realms to explore the neurobiology of multiple sclerosis.

One Nation Under Therapy: How the Helping Culture Is Eroding Self-Reliance

by Sally L. Satel, M.D., HS '88, lecturer in psychiatry, and Christina Hoff Sommers (St. Martin's Press) The authors believe that talking about problems is no substitute for confronting them. They argue that "therapism" and the "trauma industry" have begun to undermine the self-reliance and fortitude that Americans have traditionally valued.

Physicians' Cancer Chemotherapy Drug Manual 2005

by Edward Chu, M.D., professor of medicine (oncology) and pharmacology, and Vincent T. DeVita Jr., M.D., HS '66, the Amy and Joseph Perella Professor of Medicine (Jones and Bartlett Publishers) Completely revised for 2005, this handbook is a guide to all aspects of cancer chemotherapy, including a catalog of over 100 drugs commonly used in cancer treatment.

Bone Regeneration and Repair: Biology and Clinical Applications
edited by Jay R. Lieberman, M.D., and Gary E. Friedlaender, M.D., HS '74, the Wayne O. Southwick Professor of Orthopaedics and Rehabilitation (Humana Press) This collection of articles by

leading orthopaedic and craniofacial surgeons and researchers reviews the biology of bone formation and repair and the basic science of autologous bone graft, allograft, bone substitutes and growth factors, and explores the clinical application of this knowledge to patients with bone repair problems.

The Cadaver's Ball: A Novel of Revenge

by Charles Atkins, M.D., lecturer in psychiatry (St. Martin's Minotaur) Atkins creates characters with a range of motivations in this psychological thriller of the lives and loves of three medical school friends.

The Lobotomist: A Maverick Medical Genius and His Tragic Quest to Rid the World of Mental Illness

by Jack El-Hai (Wiley Publishers) In the early 1940s, lobotomy was the last resort in an attempt to relieve intractable psychiatric symptoms. This type of surgery was first performed in the United States in 1936 by neurologist Walter J. Freeman, M.D., who received his undergraduate degree from Yale in 1916, and neurosurgeon James W. Watts, M.D.—who helped pave the way for psychosurgery by conducting research on chimps at the Laboratory of Primate Physiology at Yale. The practice, now discredited, continued for more than 40 years.

The descriptions above are based on information from the publishers.

SEND NOTICES OF NEW BOOKS TO Cheryl Violante, Yale Medicine, P.O. Box 7612, New Haven, CT 06519-0612, or via e-mail to cheryl.violante@yale.edu

Personal librarians help students navigate research

Second-year medical student Kurtland Ma ran into a snag while doing research last summer in Hong Kong: he couldn't download an article on alternative HIV therapies that he'd found online. Luckily, Ma had someone to turn to—his "personal librarian" 8,000 miles away in New Haven.

That librarian was Lynn H. Sette, M.L.S., a reference librarian and one of 10 librarians at the Cushing/Whitney Medical Library paired with students in medicine, in the Physician Associate Program and in the Combined Program in the Biological and Biomedical Sciences. Just as Sette had introduced herself to Ma during his medical school orientation, each of the personal librarians meets new students as they arrive, establishing librarian-student partnerships.

When Ma sought help from Sette via e-mail in July, she sent him the article he needed. Normally, said Ma, he does well on his own. "I've done so many PubMed/Ovid searches in the past and the website is so good that I don't feel like I need all that much help—having a personal librarian seems more like a luxury," Ma wrote by e-mail from Hong Kong. "I obviously didn't expect to be asking for her help from here in Hong Kong, but now I'm starting to realize that having her is quite helpful."

Education Services Librarian Jan Glover, M.L.S., who helped create the program nine years ago, said students often turn to their librarians when they begin third-year clinical rotations. They ask for guidance—in person or by e-mail—when they're looking for "the perfect bit of information to answer a clinical question." Students also ask for help with technical problems such as downloading a medication database onto a personal digital assistant.

The most common questions are about complicated literature searches. During the past year, third-year medical student Argo P. Caminis estimated that she has asked Glover for advice two or three times a week while doing research for two journal articles on adolescent sexual behavior. Glover showed Caminis how to avoid being inundated by thousands of citations on a broad topic.

"I was getting tons of hits. She helped me to focus it by the types of journals I was looking at: whether they'd been peer-reviewed, looking for literature review articles, limiting the search to recent or relevant articles. She taught me principles of research that I think were helpful to learn early on in medical school," said Caminis, who was a co-author on an article published last spring and who will be lead author on a second. "It's a good way to reach out to students."

—Cathy Shufro

In Circulation is a column focusing on activities at the Cushing/Whitney Medical Library. Send ideas to Cathy Shufro at cathy.shufro@yale.edu.

**DOUGLAS MELTON**

In the stem cell debate, asking the right question

The intertwined debate that links abortion to embryonic stem cell research has revolved around the wrong question, said Douglas A. Melton, PH.D., co-director of the Harvard Stem Cell Institute. "I would suggest to you," he said in his keynote address at the annual meeting in May of the Associates of the Cushing/Whitney Medical Library, "that the question of when does life begin is the wrong question. The real question is: 'When does personhood begin?'"

A sperm and an egg are already alive before they meet, Melton said, rendering the notion of the beginning of life an arbitrary matter of timing. When does personhood emerge? "This is a metaphysical question that everyone should think about."

Harnessing the plasticity of stem cells and inducing their differentiation into a desired tissue is years away, Melton said, but within reach. "I predict the 21st century will be a century not about genes and DNA, but about cells and stem cell research. ... Genes are not the unit of life. Cells are the unit of life."

—John Curtis

**PHILLIP SHARP**

A new role for RNA as a regulatory molecule

In the last few years scientists have been surprised by small nucleotide sequences, microRNAs and siRNAs (small interfering RNAs), that appear to play a role in both suppressing and promoting cancer. "We are at a transition in our understanding of RNA," said Phillip A. Sharp, PH.D., Nobel laureate and Institute Professor at the Massachusetts Institute of Technology. "RNA is taking on a new role. It is a regulatory molecule."

These small RNAs are double-stranded sequences of about 22 nucleotides that act by disrupting messenger RNA. According to Sharp, they regulate up to a fifth of human genes, a function once thought to be the exclusive province of proteins. "The double strand is the signature key that converts the RNA into a regulatory molecule," Sharp said in June as he gave the Adelberg Lecture sponsored by the Department of Genetics.

This regulatory role could have therapeutic value if it can be harnessed to turn off mutant, disease-causing genes. "The big problem with using siRNAs is how to introduce them into the cell," Sharp said. "That delivery problem stands between this being a very broad platform for therapeutics and where we are at now."

—J.C.

**GLORIA STEINEM**

Research that makes women visible

Surveying a packed ballroom at New Haven's Omni Hotel in which women were disproportionately and diversely represented, renowned feminist author and activist Gloria Steinem noted the changes since she first spoke at Yale at the dawn of the women's movement in the 1960s. "The phrase *gender-specific* could have applied to all of Yale," Steinem said in April. "And *God and Man* at Yale has at least become *God and People*. There are glorious racial and ethnic and economic differences and diversity and richness. So times have really changed."

Speaking at a gala event in which she received a Women of Vision award from Women's Health Research at Yale (WHRY), Steinem lauded the work of WHRY, which supports research on sex-specific factors in health and disease. "Their questions at a time when mostly old answers rule the top are really very, very crucial," she said. "The rock-solid research that is going on makes the female half of the world visible and is clearly something we all desperately, desperately need right now."

—Peter Farley

**JOSHUA STEINERMAN**

Fuggedaboutit! Transient Global Amnesia

A 62-year-old man led a choir through a flawless rehearsal and performance, but by the end of the day he could remember none of the day's events.

He was experiencing transient global amnesia (TGA), a malady believed until the 1950s to be the product of hysteria or malingering, said Joshua R. Steiner, M.D., a senior resident in neurology who described the disorder at clinical neuroscience grand rounds in June.

Physicians now know what triggers TGA, without knowing what causes it. Triggers include swimming in cold water, sexual intercourse, an emotional event, stress and exertion. "The history and proximal events leading to the episode are crucial," Steiner said.

Episodes usually last four to six hours. Sufferers—typically people between the ages of 50 and 79—know something's wrong, but they can't recall answers to the questions they ask as they try to orient themselves.

Over the years, several theories have been proposed about what causes TGA. "None is entirely satisfactory," Steiner said. "The great thinkers who proposed mechanisms have always hedged their bets."

—J.C.

From the Middle East, in the Middle Ages

An exhibit at the Sterling Memorial Library highlights the contributions to medicine of Muslim physicians.

By Jennifer Kaylin

When we check into a hospital, take our children to the pediatrician or undergo a surgical procedure, it's likely we're benefiting from the work of medieval Muslim doctors and scholars.

"Muslims' Contributions to Medieval Medicine and Pharmacology," an exhibit of manuscripts from the Medical Historical collection at the Harvey Cushing/John Hay Whitney Medical Library, was on display in Sterling Memorial Library's exhibit corridor until September. The exhibit, said Simon Samoeil, curator of Sterling's Near East Collection, was designed to "provide positive insight" into the important contributions made by medieval Muslims at a time of high tensions between our nation and areas of the Muslim world.

In the seventh century, when former empires such as those of the Greeks, Persians and Romans fell under Arab domain, the new Islamic empire inherited many scholarly disciplines, including the developing fields of medicine and pharmacology. Recognizing their importance, Islamic leaders had works from other languages translated into Arabic, so research and study could continue.

The exhibit includes some remarkable examples of these early texts, including an illustrated Persian treatise on human anatomy, with six pages of detailed drawings. There is also a human anatomy book that was translated from Greek into Arabic by the 11th-century scholar and physician Avicenna. "His textbook was used in the West until the mid-17th century," Samoeil said.

Other artifacts in the exhibit include a medical dictionary and a book containing 31 chapters of practical information about hygiene, sexual intercourse and other topics. These Arabic translations of Greek scholarship led to later translations into Latin, Samoeil says, paving the way for Greek knowledge to become accessible to the scientists and scholars of the Renaissance.



CLENDENING LIBRARY PORTRAIT COLLECTION

In addition to these important translations, Muslims introduced new fields of medical research and clinical practice, including gynecology, embryology and a focus on the care of mothers and children. Samoeil said medieval Muslims saw the larger value in protecting the health of women.

"Women are the mothers of men," he said. "If the Arab empire was to flourish, the women needed to be healthy."

Early Arabs also contributed to the diagnosis, treatment and prevention of diseases such as smallpox and measles, and Muslim doctors were the first to incorporate surgery, then a separate discipline, into the study of medicine and to develop its practice and techniques.

Perhaps the most concrete legacy is the structure of today's hospitals, which follow the model of ninth-century Islamic hospitals. These early health care centers had open admission policies for patients of all economic backgrounds, regardless of sex, religion or ethnicity. They were run by a large administrative staff and organized into wards by gender and nature of illness. In addition, early Islamic hospitals pioneered the idea of having on-site pharmacies and training programs for students to get practical experience under the guidance of a physician.

Samoeil said the exhibit drew a favorable response from the Yale community and visitors. "The other day, I overheard three tourists," he said. "One called out to another, 'Come look at this. It's amazing. I didn't know the Arabs and the Muslims had done all this.'"

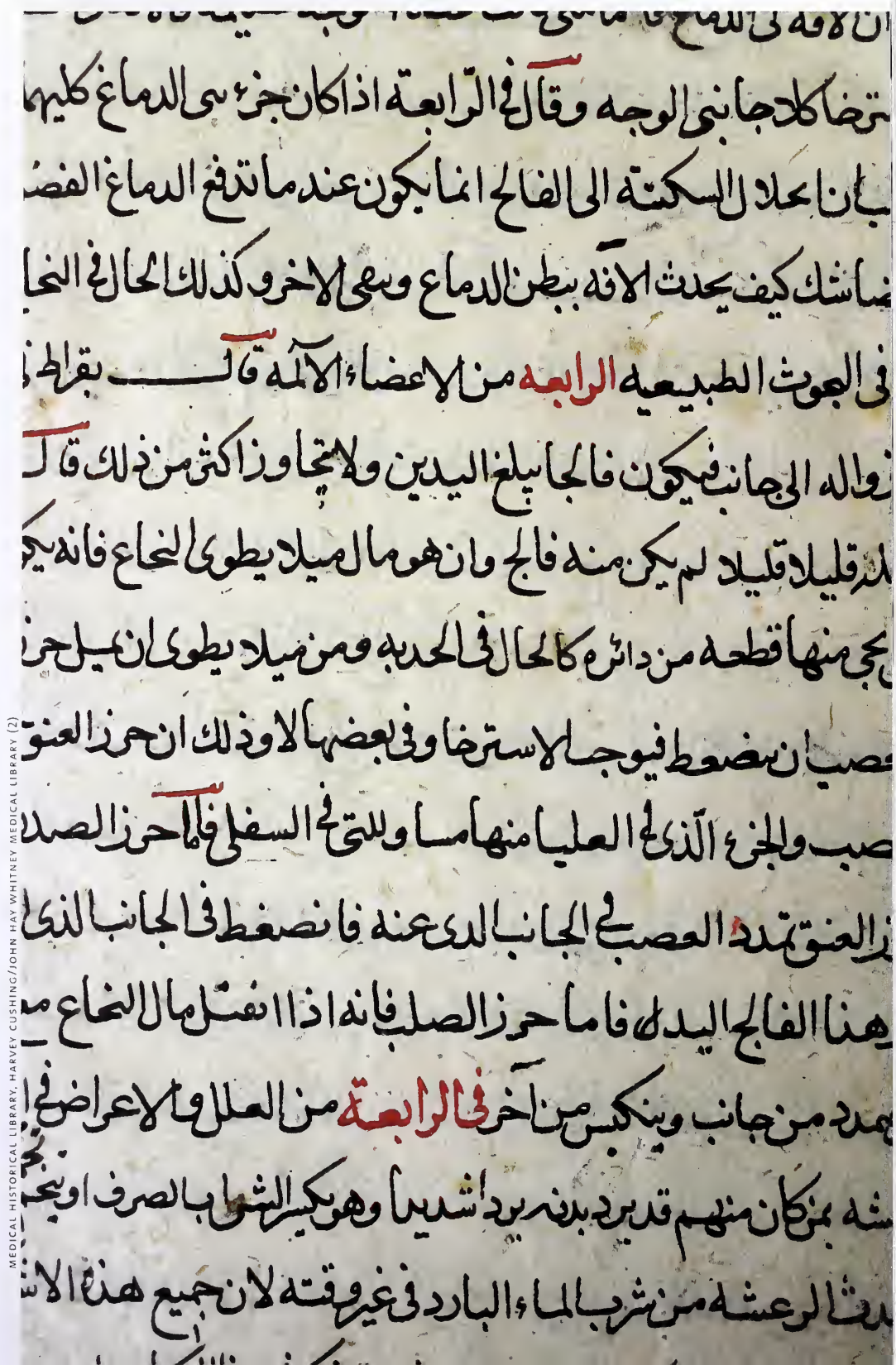
His goal in organizing the exhibit, he said, was to draw connections between the past and the present. "It's important to do that," he said. "When we look at modern materials and manuscripts, it's important to understand how we got there, to see the connection with what came before."

Jennifer Kaylin is a contributing editor of *Yale Medicine*.

OPPOSITE TOP The 11th-century Persian manuscript *Farah namah* was also known as *Ajayib al-dunya* (*Wonders of the World*). Multicolored illustrations of animals, birds, plants, stones and humans adorn the text.

OPPOSITE BOTTOM The 11th-century scholar and physician Avicenna wrote a medical text that was used until the mid-17th century.

BELOW The *Kitab al-Hawi*, believed to have been written in the 9th or 10th century, was still in use in the 1600s, when the Shah of Iran ordered it copied for his chief physician. The page shown below describes the structure of the brain as well as ailments that afflict it.



In January 2004 Johnnie Yates, M.D. '95, took a job as a physician in an international clinic in Kathmandu, the capital of Nepal. The post offered a chance for Yates to pursue his interests in travel medicine, and as he recounts in the article that follows, a typical day in his life provided insights into medicine in Nepal.

LETTER FROM KATHMANDU

Article and photographs by
Johnnie Yates, M.D. '95



OPPOSITE On the path to the base camp of the world's highest peak.

BELOW During his 18 months in Nepal, medical school alumnus Johnnie Yates took frequent trips to mountain locations, such as Poon Hill in the Annapurna Himalaya.

The rain starts innocently with scattered sprinkles—warning enough for street vendors to cover their wares and for pedestrians to seek cover. The sky darkens and the downpour begins. Rain pounding on the roof can make a telephone conversation next to impossible. And then it stops. “Must be the beginning of the monsoon,” I presume, but I learn that June is too early. Once the monsoon season (July to September) starts in earnest, the rain becomes a daily occurrence and provides relief from the heat and humidity.

Premonsoon rains herald the end of the spring trekking season, and work at the CIWEC Clinic Travel Medicine Center in Kathmandu, Nepal, slows down. CIWEC stands for Canadian International Water and Energy Consultants, the nongovernmental organization (NGO) that established the clinic in 1982. It has since become an independent center staffed by three physicians (a U.S.-trained Nepali internist, who is also the medical director, and two American doctors). CIWEC is internationally renowned for its Western standard of care and its research into the health problems of foreigners. Most patients are diplomats, staff from development agencies and NGOs, aid workers, volunteers and tourists. During busy periods the waiting room resembles a mini-United Nations, with British diplomats, Tibetan monks, Israeli backpackers and American parents and their newly adopted Nepali children awaiting consultations. Trekkers and climbers felled by altitude sickness come to the clinic as well.

I never imagined living in Nepal, a landlocked country between India and China. Apart from reading Jon Krakauer's *Into Thin Air*, about the



1996 Mt. Everest climbing disaster, or listening to Bob Seger's version of “Kathmandu,” I never thought about the place. I graduated from medical school in 1995, completed a residency in family practice at Middlesex Hospital in Connecticut, and was living in Hawaii when I received the unexpected offer to work at CIWEC. I had done medical school electives and volunteer work abroad but always preferred the tropics to the mountains. Nonetheless, the opportunity allowed me to pursue my interest in travel medicine full time. So in January 2004, I packed away my “aloha” shirts, dusted off my cold-weather clothing and moved to Nepal.

Slightly smaller than New England, Nepal has a population of approximately 25 million, with over 1.5 million people living in Kathmandu. It is best known as home to Mt. Everest, at 29,035 feet the world's highest mountain, but its lowland tropics offer a chance to go on safari in search of rhinos and tigers. The latter part of the dry season (February to May) is a popular time to visit the country, especially for trekkers and climbers.

On that rainy day in June, my first patient was Shyam, a 4½-year-old Nepali boy adopted a week earlier by an Italian couple. His cheeks had become swollen and painful over the past few days and he refused to eat.

Trekkers hike in the shadow of Mt. Ama Dablam, a 6,856-meter peak in the Khumbu region of Nepal, along a popular route to Mt. Everest Base Camp.



Both of his parotid glands (salivary glands below the ears) were swollen and tender, and he was mildly dehydrated. He also had scabies and a scalp infection, conditions present in nearly all of the children that I see from orphanages. Shyam's new parents said the orphanage had no proof of any vaccinations, thus increasing my clinical suspicion of mumps.

For a country in which the burden of infectious disease is high, diagnostic capabilities can be woefully limited. While some medical technology has reached Nepal, it does not mean that a system of modern health care delivery has come along with it. One night I had to obtain a CT scan of a patient with fever, convulsions and delirium (ultimately diagnosed as

encephalopathy due to typhoid fever). After an initial noncontrast CT at the university teaching hospital, the radiologist inquired if I wanted one with contrast, which would highlight an abscess. Upon my affirmative reply, he scribbled on a scrap of paper. Sensing my confusion, he explained that I would have to take the note to the pharmacy down the street, buy the contrast agent and bring it back for him to administer.

Shyam was stoic, even as an IV was inserted to provide hydration. I wondered what was going through his mind. He had spent most of his young life in an orphanage before he was taken away by a friendly foreign couple he could not understand. Did he realize that in one week he

would board an airplane for the first time and fly to his new home in Italy?

After I finished caring for Shyam, I called for the next patient. There was no answer from the waiting room. At CIWEC, that means that the patient is in the bathroom. Diarrheal illness accounts for a third of what we see, and the incidence increases between May and July. Regardless of how careful one is, the pathogens that cause diarrhea are impossible to avoid—I realized this after being stricken five times in my first two months in Nepal.

Bacteria are responsible for most of the diarrhea among foreigners in Nepal. However, the premonsoon season ushers in the seasonal parasite *Cyclospora cayetanensis*, which causes cyclosporiasis, a debilitating diarrheal disease characterized by marked fatigue and anorexia and first identified in Nepal in 1989 by a CIWEC lab technician.

The patient emerged from the bathroom with a big sigh and recounted how he had had intermittent diarrhea for two weeks. Every time he thought he was recovering, the diarrhea would return. He had no energy or appetite and was losing weight. His stool examination confirmed *Cyclospora*. He was treated with trimethoprim/sulfamethoxazole and reassured that his appetite should improve within a few days. Untreated, cyclosporiasis is self-limiting, but it can last up to several weeks.

After lunch Mr. Sherpa, a 40-year-old Nepali, presented with four days of fever and headache. His symptoms put typhoid at the top of the list of possible diagnoses. However, Sherpa had recently returned from the West

Bengal region of India, an area endemic for malaria. A blood smear revealed severe *Plasmodium falciparum* malaria, the most dangerous of the disease's four forms. I started an IV, administered an antimalarial and transferred him to the hospital for closer monitoring. In Kathmandu one can lose valuable time while waiting for an ambulance, so Sherpa was sent to the hospital by the quickest means available—a taxi.

As it turned out, Sherpa's ride to the hospital was held up by political demonstrations in the streets. What should have been a 15-minute ride took nearly an hour. Nepal has become increasingly plagued by political problems: an eight-year-old Maoist insurgency and a Maoist-imposed blockade of the Kathmandu valley in August 2004 made international headlines. Political parties calling for a return to a democratically elected government (dissolved by the king in 2002) frequently stage demonstrations and call for strikes. In addition to delaying patient transport, the protests can directly affect a patient's health as well—on one occasion police threw tear gas into a hospital because political agitators had fled there.

Later in the afternoon a frantic call came from Mrs. Paddington, whose husband worked for a British development agency. Her 4-year-old daughter Daisy had stuck a bead deep into her right nostril. Daisy was more preoccupied with the toys in the waiting room than the commotion that her action had caused. After a few unsuccessful attempts at blowing the bead out (by pinching off the opposite nostril and exhaling into the child's mouth, a task assigned to Daisy's

mother), I used forceps to retrieve a *bean*, rather than a bead. Mom had no idea where the bean came from, and Daisy denied putting anything up her nose. After a scolding from mom and a sticker from the nurse, she skipped happily out of the clinic. I then headed home on my bicycle.

It takes me about 15 minutes to ride home. I live in a quiet residential neighborhood a few blocks from the prime minister's residence. On the rare days when the air is unpolluted and the skies are crystal clear, I can see the Himalayas from the second floor of my house. The traffic in Kathmandu is a tangle of bicycles, motorcycles, tempos (local three-wheeled transport), cars and buses, all negotiating the congested streets. Vehicles swerve and stop without warning to avoid oblivious pedestrians, crater-like potholes and sacred cows (literally—Nepal is a predominantly Hindu country). The chaotic traffic combined with the noxious pollution frequently tests my patience, and one day I found myself laughing after I realized I had "road rage" from riding my bicycle.

As I reached my doorstep, the telephone rang. A British volunteer called to say she had been attacked by several monkeys while walking near a temple. The attack was unprovoked and, interestingly, the woman's two friends were unmolested. She had several scratches on her legs and was frightened about contracting rabies. Rabies is endemic in Nepal and monkeys are potential reservoirs. Because she had not been immunized, she required human rabies immune globulin along with a series of five vaccinations over four weeks.

Swayambhunath, a center of Buddhist thought on a hill overlooking Kathmandu, is also known as the "monkey temple," because of the wild monkeys that live nearby.



"Not your typical day back home," I mused. However, as I thought about what I had seen that day, something was bothering me. Most of the problems were preventable—mumps is rare in the United States due to routine immunizations; better sanitation and a safe water supply would prevent much of the diarrhea in Nepal; Sherpa would not have contracted malaria had he taken prophylaxis; and the volunteer's risk of rabies and her anxiety about it would have been alleviated had she been vaccinated prior to coming to Nepal. As for the bean in the nose ... well, I've seen that back home and I suppose there's no way to curb a child's curiosity. **YM**

Johnnie Yates, M.D. '95, recently took a position with Kaiser Permanente at a clinic on Oahu.

A soldier covers his head while another remains alert during an August 2004 battle with Shiite militias in the holy city of Najaf.



A photograph of a soldier in a camouflage uniform lying in a trench. The soldier is covering his face with his hands, suggesting distress or trauma. An American flag patch is visible on the soldier's sleeve. The background shows the brickwork of the trench walls.

The unseen wounds of war

As long as humans have waged war, the horrors of the battlefield have caused psychological damage. Since the war in Vietnam, this damage has had a new name—post-traumatic stress disorder.

by Cathy Shufro

A

ll but one of the 12 veterans sitting around the plastic laminate conference table appear worn and tired. Their world-weary look comes from decades in which, among them, they shot heroin, smoked and drank too much, wasted years in jail, picked fights, gambled, divorced and shuttled from job to job. They all fought in Vietnam, and more than 30 years later, as they enter their late 50s and early 60s, they are still paying the price.

Except for Luke. The former Marine is only 24 years old, 18 months back from Iraq, and he looks good. Blond, fit and handsome, he could model for a recruiting poster. But he has joined the other veterans in a United Way meeting room in Meriden, Conn., because he is hurting, too. If someone yells at him, he'll yell back, or worse. If someone steps into his bedroom, he'll smell the alien scent hours later. If someone touches him when he's sleeping, he'll attack. Thunderstorms scare him. In the months after returning from war, he went to bars, got drunk and picked fights with strangers nearly every day.

Luke provides a sense of purpose for the other vets. Guided by 57-year-old social worker and Vietnam veteran James J. Gavin, M.S.W., the older men talk about their own problems over coffee and doughnuts this morning. All, including the social worker, have been diagnosed with post-traumatic stress disorder (PTSD). For these men, the psychological and physiological adaptations that helped them to survive war persisted at home. Veterans traumatized by war—or people distressed by an event in which they fear death or great harm to themselves or others—suffer from PTSD if they meet three criteria: re-experiencing, hyperarousal and avoidance. That is, people with the disorder unwillingly revisit traumatic events in flashbacks or nightmares; they are hypervigilant, feeling irritable about trivial frustrations, constantly scanning a room or a street for danger, seeming to sleep with one eye open; and they retreat from life and

relationships because they feel emotionally numb or because they hope to avoid situations that trigger bad memories.

Gavin has helped the Vietnam veterans at the table to understand, after all these years, that they have not been messing up their lives simply because they have bad memories of Vietnam, but rather because their brains have been changed by war. The changes that helped them to survive Vietnam have made their lives back home a kind of purgatory, from the aisles of Stop & Shop to the family dinner table. The men generally took decades to realize that they had PTSD.

Gavin recognized that Luke had PTSD shortly after Luke came home in July 2003 after five months in Iraq. They met when Luke stopped by the Vet Center in West Haven, Conn., a community center sponsored by the Department of Veterans Affairs (VA), to ask about college money. During several conversations about benefits, Gavin tried to assess whether Luke had PTSD. He already knew from his Vietnam experience that many veterans come home with PTSD; a landmark study in 1988 showed that one in three men who served in Vietnam would experience PTSD. Gavin saw it in Luke and persuaded him to join the therapy group in the winter of 2004.

One of the men explains why he is glad Luke is among them. "It helps us share our experience dealing with this for 30 or more years," says Vincent, a slight man with gold-rimmed glasses and curly black hair who looks like a professor and spent a year in a homeless shelter. "Luke has the advantage of all this wealth of understanding. We didn't have any of this."

They talk mostly about feeling rage. Joe tells his story first. His huge, muscular arms are covered with many-colored tattoos, and he wears a T-shirt that reads: "When it absolutely, positively, has to be destroyed overnight: U.S. Marines." He describes the time that an elderly woman banged her supermarket shopping cart into his. Once. Twice. The third time,



James Gavin was diagnosed with post-traumatic stress disorder after fighting in Vietnam. Now a social worker, he leads other veterans in discussions of their problems.

Joe overturned the woman's cart and kicked her groceries across the floor. After security guards ejected him from the store, he rushed to his car and drove away. "I felt terrible. This poor lady just ran into me a few times."

"You can't help it," explains Craig, a mild-mannered man wearing glasses and a red sweatshirt. Vincent adds: "You have a sense of being attacked."

"You wake up one day and you're out of toothpaste, and you want to nuke the whole neighborhood," says Bob. He says that driving brings out anger in all the men at the table. But nowadays, says Bob, he stays a bit calmer when other drivers cut him off on the highway. "I've gotten better," he says with a wry smile. "I don't chase them to their doorsteps any more."

Luke is making progress, too, even though he went to the emergency room recently after he became angry at his brother and slammed his fist through a door.

"You're doing better," Gavin tells him. "Six months ago you would have hit *him*."

The 12 men around the table speak of rage and regret, of wasted years. But toward each other, they express compassion. With Gavin's help, these men are going to take care of Luke.

A malady with roots in ancient times

The deep psychological wounds of war have been documented since the time of Homer in ancient Greece. His account of the Trojan War tells of Achilles' disintegration following the battlefield death of his best friend. The psychological impact of war was called "nostalgia" during the Civil War and "shell shock" in World War I. But it was not until 1980 that the military and medical establishments in the United States formally recognized the damage done by combat stress. The age-old psychiatric illness is now called PTSD.

A Yale psychiatrist was one of the first clinicians in the nation to recognize a distinctive set of symptoms related to the Vietnam War. Arthur S. Blank Jr., M.D., HS '65, who practices psychoanalysis and psychiatry in Bethesda, Md., had spent a year in Vietnam working in hospitals in Long Binh and Saigon after finishing his Yale psychiatry residency. Soon after the war ended, Blank reviewed the charts of 60 Vietnam veterans and concluded that many had been misdiagnosed with maladies ranging from alcoholism to schizophrenia. Blank invited those men to a therapy group at the veterans hospital in West Haven, Conn., now called the VA Connecticut Healthcare System. That was in 1973, the year that most of the remaining American soldiers came home from Vietnam; the PTSD diagnosis would not be included in the American Psychiatric Association's diagnostic manual for seven more years.

"Very early on, West Haven became a center where they really understood PTSD," says Steven M. Southwick, M.D., HS '85, professor of psychiatry, who does research at the West



Psychiatrist Steven Southwick studies the neurobiology of stress responses.

Haven VA hospital. Other clinicians nationwide also began to notice the distinctive effects of war trauma that Blank had observed, and by the late 1970s, mental health professionals united to push for the official definition of PTSD.

Soon after, Yale endocrinologist John W. Mason, M.D., now professor emeritus of psychiatry, showed that the behavioral changes of PTSD had neurobiological correlates. Combat veterans with PTSD had elevated levels of stress hormones such as noradrenaline and adrenaline.

"This was a giant step," says Southwick, "because people began to understand that there was a biological basis to many of the 'psychological responses' they were seeing in people who were severely traumatized."

Since then, Yale investigators at the VA have remained at the center of PTSD research and have helped improve the care of returning veterans nationally; West Haven is home to the Clinical Neurosciences Division of the VA National Center for PTSD, whose other divisions are located in Massachusetts, Vermont, California and Hawaii. Yale researchers have found that veterans with PTSD not only undergo changes in stress hormone levels but may also have hyperreactive sympathetic nervous systems; exaggerated increases in heart rate and blood pressure; and reductions in the volume of the hippocampal region of the brain, which is critical for memory and learning.

Yale researchers are studying the neurobiology of PTSD from several vantage points. John H. Krystal, M.D. '84, FW '88, the Robert L. McNeil Jr. Professor of Clinical Pharmacology, is working with Robert A. Rosenheck, M.D., HS '77, professor of psychiatry, to study whether the antipsychotic medication risperidone helps veterans who don't respond to antidepressants like Prozac and Zoloft. Krystal is planning to investigate whether genetic factors influence how people respond to these antidepressants. C. Andrew Morgan III, M.D., associate clinical professor of psychiatry,

has worked with the military to study how military personnel respond to severe stress. He found that personnel who responded best to stress had elevated levels of neuropeptide Y, a brain chemical linked to stress.

Southwick, who is deputy director of the Clinical Neurosciences Division of the national VA PTSD center, is taking part in another PTSD study. The study is a collaboration with Deane E. Aikins, PH.D., assistant professor of psychiatry, and Maj. Paul M. Morrissey, M.D., FW '00, HS '02, a psychiatrist and chief of behavioral health at Fort Drum in upstate New York. Using functional MRI scans, they are charting variations in brain function between controls and veterans diagnosed with PTSD. Southwick says that studying the neurobiology of stress responses—and finding a physical manifestation of a psychological problem—had helped clinicians to understand PTSD better. “Before, it was all interpreted psychologically,” he says.

Depression and an adrenaline rush

Since October 2001, more than 1.1 million men and women have served in Iraq and Afghanistan, according to the Department of Defense. A research team at the Walter Reed Army Institute of Research reported in the July 1, 2004, issue of *The New England Journal of Medicine* that nearly one in six Iraq veterans and one in nine Afghanistan veterans suffered from PTSD, major depression or generalized anxiety.

Such studies provide the best window into PTSD rates, because according to Defense Department physician Michael E. Kilpatrick, M.D., “the Department of Defense would only know of those service members who reported problems and sought a diagnosis.” And many do not report their distress: in the Walter Reed study, between 60 and 77 percent of the study participants who had a mental disorder did not seek help.

The most exposed of those fighting in Iraq and Afghanistan may be members of the Reserve and National Guard, which make up 35 percent of those deployed, notes Morgan. They are vulnerable, he says, because Reservists and National Guard members generally have less training than do full-time troops. He notes that the high rate of redeployment in the wars in Iraq and Afghanistan hurts morale and increases burnout; by last summer, 280,000 of the 1.1 million had gone back, according to the Department of Defense.

Blank agrees that redeployment can intensify harm: returning for a second tour worsened PTSD for troops who served in Vietnam. “There’s some evidence that it has something to do with addiction to the adrenaline rush, which may have a physical as well as an emotional component.” (As one Connecticut veteran of Iraq described it, “Nothing can compare to it when you come home. Everything is boring. You can’t but be drawn into that intensity. Everyone I’ve talked to feels the same way.”)

The effects of trauma can last a long time. The congressionally mandated Research Triangle Institute study in 1988 that compared 1,625 Vietnam veterans with 750 other veterans and 750 civilian counterparts found that 15 years after the war’s end, 15 percent of male veterans and 9 percent of female veterans were suffering from PTSD. This compares to a rate of about 1 percent of the general population.

For those fighting in Iraq and Afghanistan, Blank predicts that the changing character of the wars will increase the rates of psychological trauma. “Unfortunately the situation in both combat zones is one of general terror,” says Blank. “There are no safe places, and as the guerrilla fighters know all too well, it’s highly psychologically debilitating to have random terror.” Blank notes that anecdotal reports suggest that at least some troops think the war is unjustified, and for those men and women “the questionable character of the war in all likelihood will contribute to the occurrence of PTSD, because there is not the buffering factor of feeling that despite the difficulties one has encountered, there is at least a sturdy justification for what one has experienced.”

Blank points out one “good-news aspect” of the situation: Reservists and National Guard members tend to be older than full-time service members, and age protects against PTSD. The most vulnerable to the disorder are 18- and 19-year-olds. Another positive aspect is that now veterans can get care much more quickly than did Vietnam vets. But the majority of veterans have historically shunned care. They avoid it in part because society stigmatizes people with PTSD, says Blank, who helped to establish and then directed the VA network of Vet Centers like the one that employs Gavin. The community-based counseling centers now number 206 nationwide.

Military officials are working against the stigma, according to Fort Drum’s Morrissey. He says that troops leave for war knowing that psychological distress is normal and that, even in a war zone, the military will provide support. That’s a big change from the military’s approach during the Vietnam War.

“The main thing that’s changed is that now the possibility of combat stress and other mental health problems, including PTSD, is mentioned up front,” says Morrissey. He says that this kind of openness is helpful, because men and women anticipating combat inevitably worry about what will happen if they fall apart. They ask themselves: “‘What if I am really scared? What if I lose it when I’m there?’ They’re all thinking about this stuff,” says Morrissey. He and his staff train soldiers how to recognize problems not only in oneself but also in others. “If they can be looking out for someone else, that helps them regain some mastery.” Making it clear that those with problems will get support, says Morrissey, “lets them push themselves a little further.”

Those who do have trouble coping can seek help from “combat stress control teams.” Stationed in the war zones, the teams are composed mostly of mental health specialists



Social worker Susan Hill helps veterans with their re-entry to civilian life.

who have completed basic training and then spent eight months studying emergency medicine and mental health care. They are backed by psychologists, psychiatrists and social workers. The combat stress control teams offer those in distress a short break and medication, if necessary. Once symptoms are mitigated, the service members return to their posts. As Luke describes it, the goal of a battlefield psychiatric evaluation is to find out: "Are you fit to pull the trigger?"

Finding help at home

Once home, veterans can seek help at a VA hospital or a VA Vet Center, says Dolores Vojvoda, M.D., assistant professor of psychiatry at the medical school and head of the PTSD and anxiety disorder service at the West Haven VA. Vojvoda says some veterans are referred by VA physicians but most call the VA for help on their own. The West Haven staff includes five part-time psychiatrists, a psychologist, three social workers, a registered nurse and three advanced-practice mental health nurses.

Vojvoda reported that by mid-summer, therapists in the PTSD clinic at the West Haven VA hospital had seen about 50 Iraq and Afghanistan veterans. She expected the numbers to grow, and the VA had recently awarded Vojvoda's group a grant to hire a new psychiatrist and two more social workers in anticipation of an influx of combatants returning with PTSD and anxiety disorders.

The VA staff provides both individual and group therapy. In the groups, veterans learn about the symptoms of PTSD and how to manage them. Treatment may also include antidepressants, sleeping pills, antipsychotic medication for intrusive memories and anger, and alpha blockers for nightmares and exaggerated startle reflex. The VA also offers programs to help veterans recover from alcohol and drug abuse, common mechanisms for coping with PTSD.

Group and individual therapists at VA hospitals often treat patients using cognitive processing therapy, a technique developed in the 1980s for rape survivors. Patients are asked

to focus on a traumatic event and to examine whether they have interpreted it realistically. For instance, a soldier may take the blame for a bad event, but the idea of fault implies some control over what happened. In reality, he or she may have been powerless to prevent what happened. The therapy also addresses overgeneralizations, such as when a person harmed by another concludes that no one can be trusted.

Therapists counseling returning service members face a paradox because so many returnees must go back to war. Susan R. Hill, M.S.W., assistant clinical professor of psychiatry (social work) at the medical school and a social worker at the West Haven VA hospital, worries about helping those with PTSD relax their vigilance if they are to be returned to a combat zone where they will once again need to be hyper-vigilant. "It's a really questionable outcome at the moment for the ones going back."

Joining a group is difficult for those with PTSD, since avoidance and withdrawal are hallmarks of the disorder. Nonetheless, says Hill, "We are convinced that there's tremendous benefit in being around folks who are dealing with re-entry." She notes that many veterans withdraw from other people, "and then they're pretty much isolated in their own heads, as we all are when we are alone, only their heads are full of carnage. ... The opportunity to speak with other people who are having trouble with re-entry breaks down the military 'strong-men-don't-cry' theory."

Luke, for one, is doing better. "You learn when you are in danger of getting set off, and you learn to avoid any kind of stress, any situation where you're going to get set off," he says.

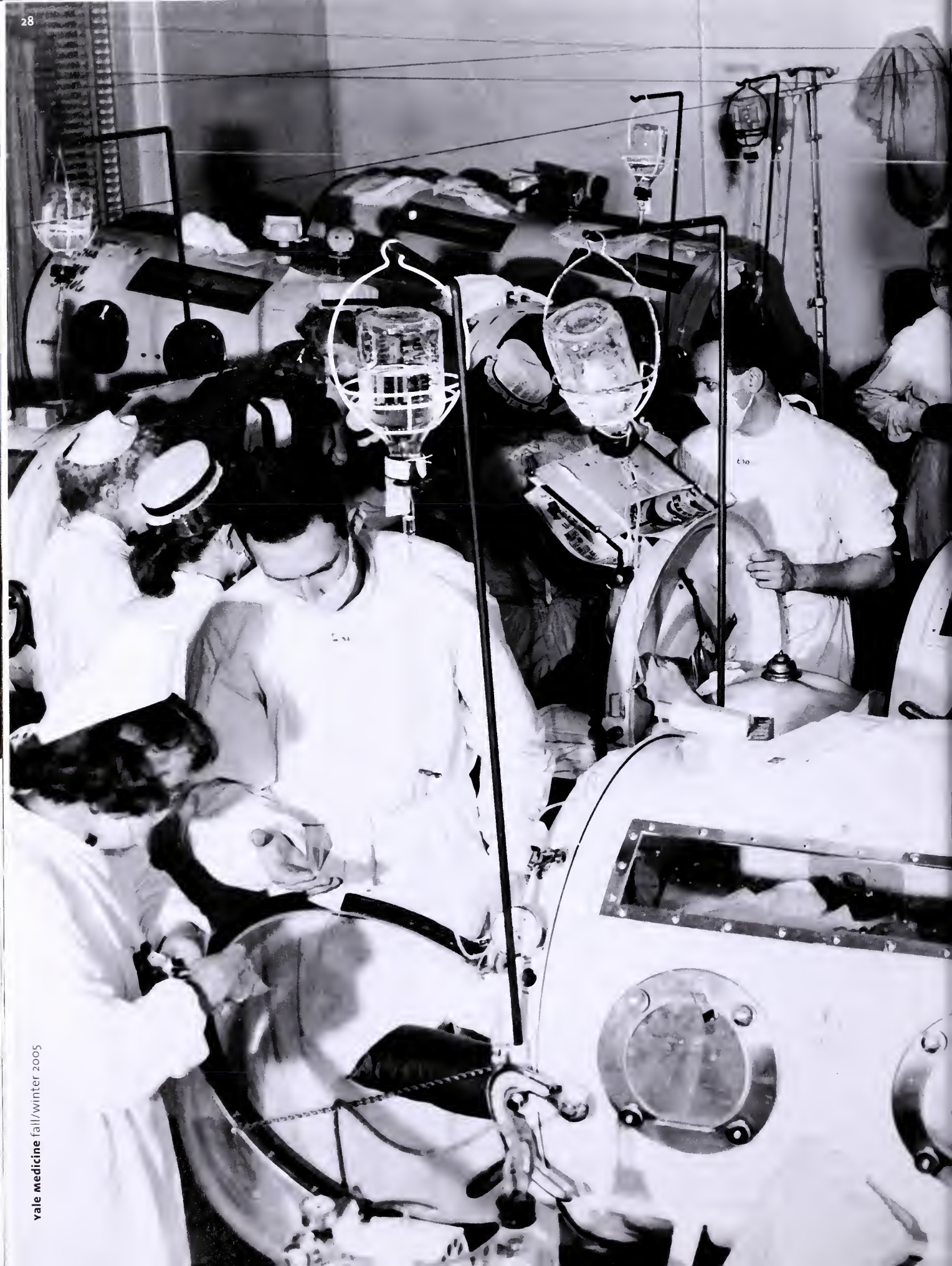
At the restaurant where he works as a cook, the boss yells at other employees—but not at Luke. "I told him when I got hired: 'You can't yell at me.'"

He told his girlfriend: "If I hit you in my sleep, I'm really sorry. If I hit you hard, I'm really, really sorry. If I'm screaming, get out quick." So far the two have co-existed peacefully in bed.

Although he finished his military service more than two years ago, Luke still toys with the idea of going back to war. He is attracted by "the rush that was associated with it. When things start going bad here, I think, 'The hell with it, I'll go back.'"

Instead, Luke has enrolled in college. He wants to emulate James Gavin and become a social worker. "I look at the way I was before I met Jimmy and how much better I am now, and I think it's a rewarding job to help somebody with what they're going through. ... He's been through the same shit I've been through, and he was my age when he did. He was in a bad place, and he pulled himself out. Now he's helping other people." **YM**

Cathy Shufro is a contributing editor of *Yale Medicine*.





Breaking the back of polio

In the 1940s, Yale's Dorothy Horstmann solved a puzzle that would lead to the first polio vaccines 50 years ago this year.

by David M. Oshinsky, PH.D.

Fifty years ago this year, following the largest public health trial in American history, a killed-virus polio vaccine developed by Jonas Salk, M.D., was found to be safe, potent and effective. The news set off a national celebration. Salk became an instant hero, the country's first celebrity-scientist, a miracle worker in a starched white lab coat. But as the years passed, the essential contributions of other researchers to this lifesaving vaccine were lost to history. Dozens of men and women had been involved—at Harvard and Yale, at Johns Hopkins and the Rockefeller Institute for Medical Research, at the University of Michigan, the University of Pittsburgh and the University of Cincinnati. What follows is the story of Dorothy Millicent Horstmann, M.D., FW '43,

Patients stricken with the most severe form of polio were confined to iron lungs, such as those seen in this ward at Haynes Memorial Hospital in Boston in August 1955.

ABOVE Dorothy Horstmann, in her laboratory in the 1970s, was the first woman to become a full professor at the medical school.

The national trial of the Salk polio vaccine began in 1954, when Richard Mulvaney gave an injection to Randy Kerr at Franklin Sherman Elementary School in McLean, Va.



whose patience and intuition produced a stunning breakthrough that made polio vaccines possible.

The story begins in June 1916, with a health crisis in Pigtown, a densely populated immigrant neighborhood of Brooklyn, N.Y. Frightened Italian parents had approached local doctors and priests, according to news accounts, “complaining that their child could not hold a bottle or that the leg seemed limp.” When the first deaths followed a few days later, health department investigators rushed to Pigtown for a house-to-house inspection. All signs pointed to a disease known as infantile paralysis, or poliomyelitis (soon shortened to “polio” by the newspapers to save headline space). As it spread from Brooklyn, communities across the Northeast closed their doors to outsiders, using heavily armed policemen to patrol the train stations and the roads. The epidemic, which lasted through October 1916, claimed 6,000 lives and left 27,000 people paralyzed. New York City alone reported 8,900 cases and 2,400 deaths, 80 percent of the fatalities being children under 5. There had been minor polio outbreaks in previous years, but nothing like this.

“The menace for the future,” warned a federal health official, “is very real.”

Polio is an intestinal infection spread by contact with fecal waste. The virus enters the body through the mouth, travels down the digestive tract and is excreted in the stool. Usually the infection is slight, with minor symptoms. In a small number of cases—about one in 100—the virus invades the central nervous system, destroying the motor neurons that stimulate the muscle fibers to contract. At its worst, polio causes irreversible paralysis, most often in the legs. Most deaths occur when the breathing muscles are immobilized, a condition known as bulbar polio, in which the brain stem is badly damaged.

Though poliovirus has long been present in the environment, the disease, unlike smallpox or influenza, had triggered no major outbreaks around the world. Why it took root in Western nations, especially the United States, during the 20th century is still a matter of debate. Some researchers pointed to more careful reporting and better diagnostic techniques. Others noted the circulation of more virulent strains of poliovirus, capable of multiplying at a ferocious rate. Still others saw a correlation between the spread of polio and the ever-increasing standards of personal hygiene in the United States—people were less likely to come into contact with

poliovirus early in life when the infection is milder and maternal antibodies offer temporary protection. Put simply, America’s antiseptic revolution brought risks as well as rewards.

A dread disease strikes at random

By mid-century, polio had become the nation’s most feared disease. And with good reason. It hit without warning. It killed some victims and marked others for life, leaving behind vivid reminders for all to see: wheelchairs, crutches, leg braces and deformed limbs. In 1921, it paralyzed 39-year-old Franklin Delano Roosevelt, robust and athletic, with a long pedigree and a cherished family name. If a man like Roosevelt could be stricken, then no one was immune.

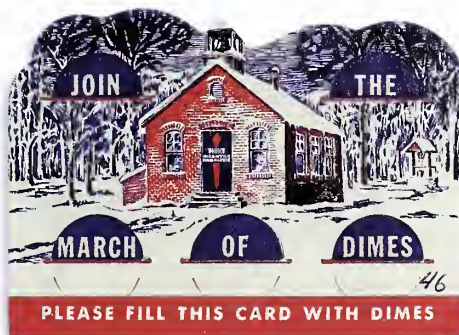
Each June in America, like clockwork, came newspaper photos of jam-packed polio wards and eerily deserted beaches. Newspapers ran tallies of the victims—age, sex, type of paralysis—akin to baseball box scores. Children were warned not to jump into puddles or share a friend’s ice cream cone. Parents checked for every known symptom: a sore throat, a fever, the chills, nausea, an aching limb. Some gave their children a daily “polio test.” Did the neck swivel? Did the toes wiggle? Could the chin reach the chest?

In truth, polio was never the raging epidemic portrayed by the media, not even at its height in the late 1940s and early 1950s. Ten times as many children would be killed in accidents in these years, and three times as many would die of cancer. What had changed following World War II was the incidence of polio in the United States as well as the rising age of the victims, a quarter of whom were now older than 10. From 1940 to 1944, reported polio cases doubled to eight per 100,000, doubled again to 16 per 100,000 between 1945 and 1949, and climbed to 25 per 100,000 from 1950 to 1954, before peaking at 37 per 100,000 in 1952. “The United States had never experienced a higher crest of the epidemiological wave,” a journalist noted of the 57,000 reported cases that year, “and never would again.”

The drive to combat polio was led by the National Foundation for Infantile Paralysis, now known as the March of Dimes. The genius of this foundation lay in its ability to single out polio for special attention, making it seem more ominous, and curable, than other diseases. Its strategy would revolutionize the way charities raised money and penetrated the world of medical research. Millions of foundation dollars would be spent to set up virology programs and polio units across the

BELOW During World War II Horstmann traveled as a member of the Yale Poliomyelitis Study Unit to Hickory, N.C., site of one of the worst outbreaks in the 20th century.

RIGHT The March of Dimes campaign allowed anyone to make a contribution. In the 1940s the campaign used a "dime card" for collections.



country, with the first grant going to the Yale School of Medicine in 1936. Although research funding went in many directions, one point became increasingly clear: the best way to prevent polio would come through a vaccine.

This was hardly a revelation. Vaccines already had proved successful against other viruses—smallpox and rabies being notable examples. But producing a safe and effective one against polio would not be easy. Three major problems had to be solved. First, researchers would have to determine how many different types of poliovirus there were. Second, they would have to develop a safe and steady supply of each virus type for use in a vaccine. Third, they would have to discover the true pathogenesis of polio—its route to the central nervous system—in order to fix the exact time and place for the vaccine to do its work.

The first problem took the longest to solve. Dozens of strains were examined, using the stools, throat cultures and, in fatal cases, nerve tissue of polio victims. Most of this work was done by ambitious young researchers hoping to attract March of Dimes grant money. (The list included Salk at the

University of Pittsburgh.) As it turned out, all of the 196 tested strains of poliovirus fit neatly into three distinct types. The poliovirus family proved remarkably, conveniently, small.

A polio vaccine, then, would have to protect against all three virus types to be successful. The next step involved the harvesting of poliovirus that was safe enough, and plentiful enough, for use in that vaccine. At Harvard, John F. Enders, PH.D., a Yale College graduate, Frederick C. Robbins, M.D., and Thomas H. Weller, M.D., using *in vitro* cultivation, grew poliovirus in non-nerve tissue—a breakthrough that would win them the Nobel Prize in physiology or medicine. By cultivating these viruses in a test tube, rather than in the brain or spinal column of a monkey, researchers could get a better look at the changes occurring in polio-infected cells. Far more important, a safe reservoir of poliovirus had now been created, free from the contaminating effects of animal nerve tissue. And that, in turn, made possible the mass production of a vaccine.

But a major problem remained to be solved. Though Albert B. Sabin, M.D., and others had speculated that poliovirus entered the body through the mouth and worked its way down the digestive tract, no one had yet discovered traces of the virus in the victim's bloodstream. How, then, did it wind up in the central nervous system? The answer would come from a research laboratory at Yale.

A girl's impossible dream in a world of men

Horstmann had a powerful fantasy as a child: she imagined herself as a doctor. Born in Spokane, Wash., in 1911, she grew up in San Francisco, where as a teenager she accompanied a physician friend of the family as he made his rounds through the local hospital. Earning her undergraduate (1936) and medical (1940) degrees from the University of California, San Francisco, Horstmann recalled that it had "never crossed my mind that [this] was in any way unusual for a woman. ... It was quite natural."

In 1941, Horstmann applied for a residency at Vanderbilt University Hospital in Nashville, where the chief of medicine, Hugh Morgan, M.D., had a strict policy of choosing only men. "I got back a polite letter, saying no," she recalled in an unpublished interview with historian Daniel J. Wilson, PH.D., of Muhlenberg College in Pennsylvania. "I wasn't exactly crushed, but I was disappointed." Six months later, while considering an offer to



BELOW Celebrities joined in the campaign against polio. In 1954 actress Grace Kelly distributed March of Dimes literature to leaders of the Mothers' March on Polio.



enter private practice in San Francisco, she received a note from Morgan asking if “Dr. Horstmann” was still interested. She was, indeed. Somehow, Morgan had forgotten that Dr. Horstmann was a woman. Horstmann later learned from his secretary that when Morgan discovered his error, he “all but went into shock. ... But we became friends, and I had a very good year there.”

When Horstmann subsequently applied for a post-doctoral fellowship at Yale, her first visit to New Haven did not go well. She had hoped to study with John R. Paul, M.D., a young pathologist who had co-founded the Yale Poliomyelitis Study Unit in 1931 with James D. Trask, M.D. As luck would have it, Paul had been called away to study a polio epidemic, leaving Horstmann to meet with Francis G. Blake, M.D., the acting dean. A giant in the field of infectious disease who was known to generations of medical students as “stuffy and remote,” Blake couldn’t quite picture Horstmann at Yale. Indeed, she recalled, he “went on to tell me how the last woman he had on the house staff did something awful.” Offended, and blissfully ignorant of the dean’s imposing reputation, she replied that “if a woman on the house staff did not live up to expectations it was remembered for the next 50 years, but if the person was a man, it was forgotten by the next year.” Horstmann was told the decision would be up to Paul. “He accepted me,” she said, “and that is how it all began.”

In 1942, with World War II under way, she arrived at Yale. As head of the Commission on Neurotropic Virus Diseases of the Army Epidemiological Board, Paul was constantly traveling to remote parts of the world. Concentrating on the spread of polio among Allied troops in North Africa, Paul confirmed the theory that adults from areas with high sanitary standards, such as Western Europe and the United States, were far more susceptible to the disease than the local population, which had built up immunity following generations of exposure.

In New Haven, Horstmann joined the Yale polio unit. Missing its two founders—Trask died of a bacterial infection in 1942 while working at an Army camp—the ranks included a handful of superb researchers, such as Joseph L. Melnick, M.D., and Robert Ward, M.D. Using an approach pioneered by Paul and known as “clinical epidemiology,” the polio unit, including Horstmann, tracked polio epidemics in Connecticut, Illinois, New Jersey, western New York state and Hickory, N.C., site of one of the worst outbreaks of the 20th century. The unit tested water and sewage, trapped flies and other insects and took blood samples from those who had the disease and those without symptoms, hoping to discover both the route of poliovirus through the body and the manner of transmission from one person to another. For Horstmann, who had come to Yale to study *Streptococci*, the switch to polio was inspiring. “It had a dramatic immediacy,” she said. “When you deal with an epidemic you realize it’s an urgent thing. There was so much to be learned.”

Tracking polio’s pathogenesis

Like others in the polio group, Horstmann combined her clinical studies with laboratory research. During a polio epidemic in New Haven in 1943, she collected blood specimens from every patient admitted to the hospital with symptoms of the disease—111 in all. Only one tested positive for poliovirus, a little girl with minor neck pain. Was it possible, Horstmann wondered, that poliovirus was only present in the bloodstream during the brief period before a victim took sick and the physical symptoms became apparent?

To test this theory, she began a series of experiments on monkeys, feeding them poliovirus by mouth to determine if, and when, it turned up in their blood. The results were dramatic. Poliovirus was detected within days of the feed-

BELOW LEFT Braces and the iron lung became symbols of the feared disease. The epidemic reached its peak in the early 1950s, climbing to 37 cases per 100,000 in 1952.

ings. Why had so many others failed to discover this? The answer was deceptively simple: they had waited too long before looking. Horstmann's discovery, published in 1952, would pave the way for both the Salk killed-virus polio vaccine and the Sabin live-virus polio vaccine.

Working independently at Johns Hopkins, researcher David Bodian, PH.D., M.D., later reported almost identical results. When poliovirus enters the blood, it creates the very antibodies that will soon destroy it, wiping away the signs of its existence. Horstmann had determined the time (early in the infection) and the place (the bloodstream) for the battle against polio to be waged. Her findings meant that an immunizing vaccine, packing low levels of antibody, could destroy the virus before it entered the central nervous system. In a personal letter to Horstmann in 1953, John F. Fulton, M.D., D.PHIL., Yale's distinguished historian of medicine, proclaimed: "This disclosure is as exciting as anything that has happened in the Yale Medical School since I first came here in 1930 and is a tremendous credit to your industry and scientific imagination. ... It is also medical history."

BELOW RIGHT This 1953 cartoon offered simple instructions for avoiding poliovirus.

That history would continue. In 1959, the World Health Organization sent Horstmann to the Soviet Union, Czechoslovakia and Poland to evaluate the massive public health trial involving Sabin's oral polio vaccine. Her favorable report led the way to its licensing, and widespread acceptance, in the United States and beyond. Worldwide the incidence of polio fell to 1,919 cases in 2002, a decline of 99 percent since 1988, when 350,000 cases were reported. The United States has not seen a case of wild polio since 1979.

In later years, Horstmann became the first female professor of medicine at Yale (1961), the first woman in the university to hold an endowed chair (1969) and an elected member of the National Academy of Sciences (1975).

Horstmann died in 2001. Today her portrait hangs at the School of Medicine in a gallery of luminaries from the 19th and early 20th centuries. She is the only woman honored on these walls. **YM**

David M. Oshinsky, PH.D., the George Littlefield Professor of American History, University of Texas at Austin, is the author of *Polio, An American Story: The Crusade That Mobilized the Nation Against the 20th Century's Most Feared Disease*, published this year by Oxford University Press.



POLIO PRECAUTIONS

Gamma Globulin—obtained from human blood—gives protection for a few weeks. However, it is in **VERY SHORT SUPPLY**.

A vaccine is not ready for 1953. But there is hope for the future.

Meanwhile—when polio is around—follow these **PRECAUTIONS**.



RECOMMENDED BY THE NATIONAL FOUNDATION FOR INFANTILE PARALYSIS





Dean Robert Alpern has spent his first year at Yale getting to know the medical school and bringing the faculty together in a strategic planning process.

A year at the helm

Since he arrived at Yale in 2004, Dean Robert Alpern has led faculty to a new vision of the medical school, with a focus on clinical expansion and the application of great science.

By Michael Fitzsosa

It's 8 a.m. on a Wednesday morning in late July, and Robert J. Alpern, M.D., has assembled his senior leadership group for its weekly meeting. About halfway through today's agenda, the five people at the table are discussing options for an electronic medical record, or EMR. The computer-based patient chart is becoming a must-have in medicine's transition to the digital age. Computerized record-keeping lessens the likelihood of a mistake being made—preventing a medication from being prescribed at a dangerous dosage, for example, or ordered for an allergic patient. It also holds promise for clinical researchers hunting for patterns in the illnesses, interventions and outcomes of patients, to determine which treatments work best for which groups of individuals.

The problem is that the medical school and its affiliated practice and hospitals do not yet share an EMR or a data repository, the computerized warehouse where data from medical visits, tests and surgical procedures are stored. There are competing software products, a still-shifting technology platform, major costs to implement and maintain a system and many questions remaining about how to get doctors to adapt to new ways of charting patient information and ordering drugs and tests. A central dilemma, Alpern notes, lies in

the trade-off between ease of use and specificity: the systems that are most practical for physicians are the least useful for researchers, while those that standardize data entry in a way that makes sense for research are unwieldy for busy doctors.

This issue is just one of eight or nine broached at today's weekly meeting, unusual in that the agenda is fairly short. Some weeks it grows to as many as 25 or 30 items, all of which need to be moved forward during the three-hour session. Today's topics include the potential reorganization of one of the academic departments, planning for a new center for clinical research, two or three new fund-raising opportunities, a review of the medical school's website, the retreat for department chairs in the fall, a proposal for a student-run free clinic and renovations to the school's day care facility. Alpern, a nephrologist and Ensign Professor of Medicine, moves things along but allows the discussion to meander enough to pull in many points of view. From time to time, he takes an index card out of his shirt pocket and jots down a few words on the back of his schedule for the day.

The talk eventually leads to the perennial space crunch at the medical school and the constant juggling of lab, office, clinical and teaching space inherent in managing a growing

institution of 1,787 full-time faculty members, 1,150 students and more than 3,000 full-time employees. Two years ago the 457,000-square-foot Anlyan Center opened on Congress Avenue, and a new, smaller building on Amistad Street is almost complete, but still there is not enough room for new programs and people. Space is at such a premium that Alpern holds a weekly meeting to work on the ever-changing puzzle. "Everything is so dependent on facilities, and you

view but is enough of a pragmatist to know that a higher ranking will help the school attract the best faculty and students.

He also has two giant tasks ahead of him: leveraging Yale's formidable strength in the basic sciences to translate knowledge about molecules and cells into new ways of treating illness, and putting those treatments to work in a much larger patient base. Yale has long been known as a powerhouse in biological science but has not had the same scope

"Everything is so dependent on facilities, and you always have to think years in advance. I still think we're one building away from where we need to go."

always have to think years in advance," he says. "I still think we're one building away from where we need to go."

Before the discussion draws to a close, Alpern excuses himself to take a call, a rare interruption of the weekly meeting. As it turns out, the occasion is anything but ordinary: a successor to Joseph Zaccagnino, M.P.H. '70, the president and CEO of Yale-New Haven Hospital (YNHH, the school's primary teaching hospital and clinical partner), has been named and will be announced later in the day.

Opportunity in New Haven

Alpern came to Yale the summer before last from the University of Texas Southwestern Medical Center. Dallas is a world away from New Haven in its geography, politics, culture and climate, but it shares a rich tradition in science with the medical school. It was a young Yale medical graduate, Donald W. Seldin, M.D. '43, HS '46, who transformed the Southwestern campus from a compound of Quonset huts in the 1950s to the powerhouse in basic science and medical research that it has become. Alfred G. Gilman, M.D., Ph.D., the Nobelist who succeeded Alpern as dean there, is a Yale College alumnus and son of one of the Yale pharmacologists who developed the first chemotherapy treatment for cancer in the 1940s.

Alpern was recruited to Yale not only to lead a world-class medical school with an annual budget of more than \$750 million, but also to counter several unsettling trends, including a mounting operating deficit (\$35 million in fiscal 2004) and a general perception that the school was beginning to slip in relation to some of its peers. Third in funding to medical schools from the National Institutes of Health in 1993, the school still brings in more than \$260 million in federal grants, but gradually dropped to eighth place during the 1990s and early 2000s as other schools were expanding their campuses and research capacities. Its ranking in the *U.S. News & World Report* annual survey of research medical schools dropped from third in 1996 to 11th this past June. Many academicians dismiss the rankings, arguing they lack scientific rigor and rely too heavily on subjective assessments—reputation in particular. Alpern understands that

and depth in clinical practice, despite a handful of subspecialties that attract patients from outside the region, a few of them internationally. Alpern wants to expand the medical school's programs in cancer care, cardiovascular medicine, organ transplantation and other key areas of practice to raise Yale's profile nationally.

His honeymoon period as dean may still be in effect, but many faculty members are pleased by what he has done in his first year. Robert Udelsman, M.D., M.B.A., the Lampman Memorial Professor of Surgery and Oncology and chair of surgery, says Alpern is "available, approachable and affable, and he appears willing to delegate to others and empower them." With the appointment of a new hospital CEO—Marna P. Borgstrom, M.P.H. '79 (See *Chronicle*, p. 5)—and a new dean at roughly the same time, Udelsman says, the medical center is presented with an unusual opportunity.

"Here is the entrée for Yale-New Haven Medical Center to make a fundamental decision about what it wants to be, whether it wants to be the best [medical center] in the world—not just in the top 10, but number one," Udelsman says. "The hospital can't do it alone, and the medical school can't do it alone."

David L. Coleman, M.D., HS '80, the interim chair of the Department of Internal Medicine, says that Alpern worked hard during his first year on the school's relationship with YNHH, the recruitment of department chairs and the launching of a strategic planning process that occupied 70 faculty members on three committees from last December until August. Throughout the planning process, Alpern dropped in on meetings and participated in the discussion, helping guide it at times but mostly listening. "I would say the key word to my management style is consensus building," he says. "I don't try to force people to do things. I try to think things out so that I have a vision for where we should go, and then I try to build a consensus."

Planning for the future

Alpern sees the strategic planning effort, which was shared by three committees evaluating basic science, clinical practice and clinical and population-based research, as a major contributor

to the healthy functioning of the medical school. (A fourth committee has been evaluating the educational mission in a separate process.) "Two of the best things that have come out of it are communication and the creation of a common sense that the institution has a direction," he said in an interview in late summer, as the final reports were being circulated among the planning groups and edited into final form. "In a university, you have each faculty member marching to the beat of

tive and convenient for patients without dampening the entrepreneurial spirit that has driven progress in the specialties and subspecialties.

"The faculty at Yale in general are all excellent doctors, but in many cases we don't have enough of them to provide good service to our local and more national constituency. In addition, we don't have the mechanisms in place to provide such service," Alpern says. Patients should be able, with

"We need to become a very user-friendly medical center that patients can navigate easily and where they can uniformly receive the highest level of care."

his or her own drummer, and if you get the best faculty, that works. But an institution should also have a sense of direction, and people felt we didn't."

Among the recommendations to come out of the planning process was the establishment of large multidisciplinary programs in stem cell biology, cardiovascular medicine, cancer, genetics and the neurosciences. The planners also identified areas of infrastructure that needed strengthening, as well as strategic "cores," or pooled resources, to provide the latest technology and expertise to faculty conducting research. One example, discussed at the dean's group meeting, is a center for clinical and population-based investigation bringing together the statisticians, study designers, computer scientists, regulatory professionals and others who are essential to the conduct of large studies evaluating new drugs and medical procedures.

From the basic science committee, the dean received recommendations for expanding or starting academic programs as well as bolstering certain portions of the academic infrastructure. For example, the group urged expansion of the Combined Program in the Biological and Biomedical Sciences (which has unified graduate education across the medical school and central campuses) and investment in animal facilities, X-ray diffraction equipment for structural biologists, laboratories for drug development and testing, small-molecule screening systems, RNAi screening (a hot technology that promises to identify potential new drug targets many times more quickly than previous methods) and advanced biomedical imaging.

The clinical committee focused on even more basic infrastructure: mechanisms for improved planning, communications, marketing and support services, as well as an EMR and a central scheduling service to standardize the way appointments are made. Like many medical schools, Yale saw its clinical departments grow quickly in the 1970s, '80s and '90s with an autonomy that would surprise many outsiders. For years, each ran its own ship and handled its own scheduling and administrative operations. Now the challenge is to make sure the system as a whole works in a way that is effective

ease, to make appointments, schedule tests, obtain results, see multiple specialists and count on good communication among them and their referring physicians—things that cannot always be taken for granted, Alpern says. "We need to become a very user-friendly medical center that patients can navigate easily and where they can uniformly receive the highest level of care."

That task has been entrusted to David J. Leffell, M.D., HS '86, the newly appointed deputy dean for clinical affairs, who has been the driving force behind the 750-member Yale Medical Group since 1996. Other members of the senior leadership team are Jaclyne W. Boyden, M.B.A., the deputy dean for finance and administration; Carolyn W. Slayman, Ph.D., the deputy dean for academic and scientific affairs; Martha E. Schall, M.B.A., the university's associate vice president for development and director of medical development and alumni affairs; Mary J. Hu, M.B.A., the director of planning and communications; and Julie B. Carter, J.D., an associate general counsel of the university.

Alpern cites the formation of the leadership group as one of the most important accomplishments of the past year. The group provides a structure for dealing with the complex problems the medical school must deal with, the EMR being just one example from this week's meeting. "The problem is, it could be very easy. We could go real fast and do it wrong," he says of the EMR process. To make good decisions, Alpern does what most corporate CEOs would do and works closely with a small group of senior leaders in whom he has complete confidence, delegating authority to them. There is a twist, however.

"Most people would tell you that you should have no more than about six direct reports, and unfortunately, that's where the system breaks down in academics," he says. Such a business model would have the 27 academic departments reporting to one of the deputy deans, but Alpern says. "I couldn't stand that model. It removes the dean from the academic presence of the medical school, and it would frustrate any good chair. Plus it would take me out of what I consider some of the most enjoyable

parts of the job." Instead, Alpern meets weekly with his core group and at least biweekly with the department chairs. If something comes up, he adds, "any chair can get on my calendar within a week." A newly formed dean's advisory group of senior faculty will assist in major decisions affecting the school. In addition, Alpern has scheduled regular meetings with the departmental faculty so that he visits with each department once a year.

If the bottom line drove every decision and no investments were made, it would be a disaster.

A long commute

Alpern is married to nephrology researcher Patricia A. Preisig, M.S., PH.D., who remained in Dallas for the first year of his deanship, while their daughter, Rachele, finished high school (she entered Yale as a freshman this September, and their son, Kyle, is a sophomore at the Hopkins School in New Haven). Alpern spent the first year commuting home on the weekends to Dallas, where he held his weekly lab meeting—he moved his nephrology lab to Yale in August—and took up tennis again after many years, joined by his son. Originally from Long Island, N.Y., where his parents and his sister and her family still live, Alpern says he was happy at Southwestern but was attracted both by the opportunity to come to Yale because of its position as a leading medical school and by the chance to help solve its problems.

"I wouldn't have moved for a school that wasn't as good as Yale," he says, "and I'm not sure I would have come if it was not a chance to really put my fingerprint on Yale."

He sees empowering the clinical faculty as one of the most important tasks before him. He and Leffell speak daily about clinical issues and have put a great deal of effort into building up the Yale Cancer Center (more than a dozen cancer clinicians have been recruited in the past year), relaunching the school's liver transplant program and placing faculty who are primarily clinicians on an equal footing with their counterparts in research. Getting promoted at a top medical school traditionally has hinged on prowess in the lab, for scientists and clinicians alike, but in recent years Yale and some of its peer institutions have introduced new faculty tracks that reward clinical excellence. Last year, Yale lifted its cap on the number of faculty in one of these categories, the clinician-educator track, because Alpern felt the clinical practice could not grow otherwise. "I told the provost, there's no choice here. We must lift this cap, and [then-Provost] Susan Hockfield said okay," he says. "Anyone who's really an outstanding clinician and educator who has a national reputation will be promoted to professor. And when you're a professor here, your title doesn't say what track you're on. All people

know is that you're a professor. I really believe all the tracks are equal."

Teaching is also of critical importance to the school's future, and Alpern says Yale has one of the best educational programs in the world. "The Yale System, I think, is great, in that it allows the students to focus on learning rather than on grades and to explore their own unique interests through the thesis. It's just terrific. It's how you create the leaders of tomorrow."

Alpern says the least pleasant parts of the dean's job are the schedule—he has meetings from 8 a.m. to 7 p.m. most days, is out several evenings a week, answers e-mail late into the night and works through the weekends—and getting and dealing with bad news. For example? "Faculty who want to leave," he says. "That's probably the most unpleasant and the most important to deal with. When you have a great faculty, they're constantly under attack" by competing schools wanting to recruit them. He is also under pressure to balance the budget while making major investments in the school's future. Those two goals might seem contradictory, but Alpern says they go hand in hand. Cost containment is a critical piece of the equation, and so are fund-raising and a policy of well-thought-out expansion. If the bottom line drove every decision and no investments were made, he says, it would be a disaster.

Encouraged by his first year, Alpern says he has no doubt the school will reach its goals. From his perspective, the good days in the dean's office outnumber the bad days by a wide margin. "I'd say the proportion is about 10 to 1, good days to bad," he says.

Is he serious about that ratio? Well, yes, Alpern says, while acknowledging the extreme sunniness of the estimate. "You have to understand, I'm an optimist," he adds. "You can't ignore some of the bad news, but I try to focus on the good things." **YM**

Michael Fitzsosa is the editor of *Yale Medicine*.



A half-century of change

A retired pathologist looks back on 50 years of evolution in medicine and what it means for the future.

Reminiscing about the world of medicine my colleagues and I entered 50 years ago is like flipping through old *Life* magazines. Not only has everything changed, but the rate of change continues to accelerate. I have seen these changes in my work as a laboratory director at an inner-city teaching hospital, where I have been responsible since the early 1960s for introducing new technologies. I have also been an ambivalent witness to the extraordinary transformation of the landscape in health care delivery.

My first clinical laboratory was really an extension of those encountered in college premedical programs. There were guinea pigs, frogs and rabbits for microbiology. Photometers were just replacing the human eye for evaluating the color changes in chemical reactions. Of the 40 tests we offered, we had done about half as medical students. Fast forward: like most middle-size hospitals, mine now offers more than 2,000 diagnostic tests, with 375 done in-house. Analytical systems are automated, from order entry to printing charts. Units of measure have shifted from grams to picograms or parts per billion. The original "big three" studies in radiology—the chest film, gall bladder series and barium enema—have been replaced by MRIS, PET and CT scans.

When I graduated from Yale in 1956 the physician-patient relationship was usually one-on-one. House calls

were common. There were eight medical specialties. Physicians generally knew all 20 or so major drugs. Office records were kept on 5-by-7 cards, and \$3 in cash covered an office visit. My original malpractice bill for \$100,000 per incident/\$300,000 per year was \$24. Bureaucracy and paperwork were minimal and overhead expenses negligible. Insurance companies paid fees without hassle, and the clinician had autonomy to make medical decisions.

By the '60s and '70s massive expenditures in research began to generate new knowledge, new technologies and sometimes unrealistic expectations. Younger, procedure-oriented subspecialists were riding the crest of the wave. However, the bulk of physicians, mostly older generalists, were less fortunate. Many found themselves caught in a tangle of double-digit overhead expenses, fixed reimbursement schedules, new mandates, audits, benchmarks, business models in which patients are "customers," electronic records, "keeping up" and gloves-off competition for patients. By the late '80s, for some clinicians, compensatory mechanisms that had allowed them to maintain the status quo began to break down, sweeping away the lives they had known. Once unthinkable, "denying access" became a reality. Symptoms of "burnout" were growing. Some clinicians have retired early. Some, though disgruntled, plod on. Others have, for the first time, become active politically, especially to effect tort reform. Many physicians warn students not to go into medicine!

The two great forces that changed our professional lives—new knowledge and limited resources—will have an even greater impact on those now

entering the system. Consider this: The best estimates are that, worldwide, \$90 billion annually is being spent on research and development in the biological sciences—producing some 8,500 articles per day! And with the national debt growing and with the fiscal integrity of Social Security, Medicare and Medicaid threatened, massive increases in health care funding are unlikely. These two forces will keep the lives of young physicians in perpetual turbulence.

Yet I do not see the future of medicine as bleak. The core mission of medicine, enunciated throughout the ages, endures. The basic needs of the human race are not changing. What will continue to change are the technology and the organizational framework, including financing, by which the potential of this technology will be made available to society as a whole. Fortunately those entering the system are already developing the necessary survival skills: they know they must keep learning and adapting, and they have expectations attuned to the current system. Some will come to understand the need to get active politically. They will not be caught unprepared, as our generation was, for the rapid transformation of health care. They enter the profession expecting change.

Dwight F. Miller, M.D. '56, HS '58, is an associate clinical professor of pathology at the School of Medicine.

WE WELCOME SUBMISSIONS

Do you have an opinion to share on a vital topic in medicine, health or science? Send your thoughts to Essay, *Yale Medicine*, P.O. Box 7612, New Haven, CT 06519-0612, or via e-mail to yymm@yale.edu.



Gail D'Onofrio

D'Onofrio named head of emergency medicine

GAIL D'ONOFRIO, M.S., M.D., associate professor of surgery (emergency medicine), has been named section chief of emergency medicine at the medical school and chief of adult emergency services at Yale-New Haven Hospital. She had led both services in an interim position since 2004.

D'Onofrio practiced nursing for many years before getting her medical degree in 1987. She chose emergency medicine, she said, for the excitement of making a radical difference in patients' lives, literally in seconds. She calls her practice one of "controlled chaos" and acknowledges that it takes a particular personality to cope. In addition to her clinical work, she has done research on using the emergency department to move alcohol and drug abusers into treatment. She recently received a \$3.6 million grant from the National Institute on Alcohol Abuse and Alcoholism to test a counseling intervention with harmful and hazardous drinkers. Half of all major traumas are alcohol- or drug-related, so addressing substance abuse can prevent visits to the emergency department.

In her dual roles she manages emergency departments on-site and at a satellite clinic in Guilford, Conn., and conducts research, teaches medical students and is responsible for emergency physicians in residency. She is also medical director of Women's Heart Advantage, a New Haven-based program aimed at educating patients and clinicians about the risks of cardiovascular disease in women. And she heads Project ASSERT, a program in which health promotion advocates screen emergency department patients for drug and alcohol abuse.



Carolyn Slayman

Fund honors a mentor, boosts young scientists

When Applera Corp. of Norwalk, Conn., asked members of its board of directors last spring to suggest recipients for gifts from the company, CAROLYN W. SLAYMAN, PH.D., the medical school's deputy dean for academic and scientific affairs and a member of Applera's board, suggested a grant that would also promote her ideals in biomedical education.

Slayman earmarked \$300,000 to endow a fund that will support Yale's Combined Program in the Biological and Biomedical Sciences (BBS) and honor the memory of her mentor and thesis advisor, Edward L. Tatum, PH.D. She met Tatum at Rockefeller University in New York City, where she earned her doctorate under his supervision in 1963, a few years after he won the Nobel Prize in physiology or medicine for pioneering work on genetic regulation of metabolism in the cell. "For a very famous man—he was at the height of his career—he nonetheless took extraordinary measures to work closely with every student and every postdoc in his lab group,"

recalled Slayman, Sterling Professor of Genetics and professor of cellular and molecular physiology.

Tatum, who died in 1975, did part of the research that led to the Nobel while he was on the Yale faculty. Tatum and his graduate student Joshua Lederberg, PH.D. '47, who shared the prize, along with Harvard geneticist George Wells Beadle, PH.D., discerned how bacteria exchange and recombine genetic material, findings that paved the way for gene sequencing and genetic engineering.

Ever the scientist, Slayman said she hopes the Applera gift will be "autocatalytic"—a term from chemistry for the mechanism by which the products of a reaction provide fuel for further reactions—and will inspire others to support the BBS program. Applera's contribution already shows signs of self-replication: it stands to benefit from a university policy that matches endowment gifts to the School of Medicine, which will double its impact.

Applera is the parent company of Applied Biosystems, which develops and markets scientific equipment, and Celera, which played a major role in sequencing the human genome.



Edward Zigler

Center renamed in honor of "father" of Head Start

At a celebration in July, the Yale Bush Center in Child Development and Social Policy was renamed in honor of EDWARD F. ZIGLER, PH.D., Sterling Professor Emeritus of Psychology, considered the "father" of the Head Start program. Zigler was also the founder of the center, now called the Edward Zigler Center in Child Development and Social Policy.

The center is one of the nation's oldest centers for child and family policy research. It has been part of the Department of Psychology and the Child Study Center, where it serves a critical role in training and scholarly research.

Walter S. Gilliam, PH.D., assistant professor at the Yale Child Study Center, who has been affiliated with the Zigler Center since 1995 and is known for his studies of state-funded prekindergarten systems, has been named director of the center. Matia Finn-Stevenson, PH.D., will remain as associate director, and Sandra J. Bishop-Josef, PH.D., will continue as assistant director. Zigler will serve as director emeritus.

Zigler is regarded as the nation's leading researcher of programs and policies for children and families, having planned or implemented such national programs as Head Start, Early Head Start and the innovative School of the 21st Century. Founded by Zigler in 1978 with funding from the Bush Foundation of Minnesota, the center works to improve the lives of America's children and families by bringing the results of empirical research on child development into the policy arena.



Edward Tatum

**Henry Binder****Alison Galvani****Theodore Holford****Akiko Iwasaki****Glenn Micalizio****Lynne Regan****Sandra Resnick****Raymond Yesner**

Sandra L. Alfano, PHARM.D., an associate research scientist in the department of medicine, has been appointed chair of one of the medical school's two institutional review boards for research involving human subjects. As chair of Human Investigation Committee I, Alfano is responsible for overseeing several hundred research protocol applications a year.

Roland E. Baron, D.D.S., PH.D., professor of orthopaedics and rehabilitation and of cell biology, received the D. Harold Copp Award from the International Bone and Mineral Society in June, for "outstanding achievements in basic research in the fields of bone and mineral metabolism that have led to significant changes in understanding of physiology or disease."

Henry J. Binder, M.D., professor of medicine (gastroenterology) and of cellular and molecular physiology, received the 2005 Distinguished Achievement Award from the American Gastroenterological Association in May. The award honors his research into the pathophysiology and treatment of diarrheal diseases.

Joyce A. Cramer, B.S., associate research scientist in psychiatry, was elected in May to the board of directors of the International Society for Pharmacoeconomics and Outcomes Research, an organization dedicated to translating research into practices that lead to efficient and equitable allocation of scarce health care resources.

Stanley J. Dudrick, M.D., professor of surgery (gastroenterology), received the 2005 Jacobson Innovation Award from the American College of Surgeons in June. He was honored for his contributions to science, medicine and education through his research and achievements in nutritional support for surgical patients. In 1967 Dudrick demonstrated that infants could receive nutrition intravenously and still grow and develop.

Alison P. Galvani, PH.D., assistant professor of epidemiology (microbial diseases), received a Young Investigators' Prize in June from the American Society of Naturalists for her work in evolutionary ecology.

Theodore R. Holford, PH.D. '72, the Susan Dwight Bliss Professor of Epidemiology and Public Health and head of the division of biostatistics, was elected a fellow of the American Statistical Association.

Akiko Iwasaki, PH.D., assistant professor of immunobiology, is one of 11 recipients of the 2005 Burroughs Wellcome Fund Investigator in Pathogenesis of Infectious Disease Award, which will allow her to study the role of mucosal lining cells in the initiation of immune responses against viral infections.

Becca R. Levy, PH.D., associate professor of epidemiology (chronic disease), has been named a fellow in the Behavioral and Social Sciences section of the Gerontological Society of America. Fellows are recognized by their peers for outstanding contributions to the field of gerontology.

Judith H. Lichtman, PH.D., M.P.H. '88, assistant professor of epidemiology (chronic disease), received the Women with Heart Research Award in June from the American Heart Association for her work on her research grant "Prospective Registry for the Predisposing Factors, Care and Outcomes of Myocardial Infarction in Young Women."

Glenn C. Micalizio, PH.D., assistant professor of chemistry, has been named a 2005 Beckman Young Investigator. The Young Investigator Awards are given annually by the Arnold and Mabel Beckman Foundation to support promising young faculty members in the early stages of their careers in the chemical and life sciences.

Linda M. Niccolai, PH.D., assistant professor of epidemiology (microbial diseases), received a three-year, \$240,000 grant from the Patrick and Catherine Weldon Donaghue Medical Research Foundation to examine sources of repeat chlamydia infections in young women. Niccolai's multidisciplinary study, which will continue through 2007, will provide a more complete understanding of the factors that influence the trajectory from initial diagnosis to repeat infection.

Lynne J. Regan, PH.D., professor of molecular biophysics and biochemistry and of chemistry, has won a fellowship from the John Simon Guggenheim Memorial Foundation for her studies of novel anticancer reagents.

Sandra G. Resnick, PH.D., assistant professor of psychiatry, received the 2005 U.S. Psychiatric Rehabilitation Association Carol T. Mowbray Early Career Research Award, one of five presented by the association for outstanding contributions to the field of psychosocial rehabilitation. Resnick is the associate director of the Northeast Program Evaluation Center of the Veterans Health Administration.

Steven M. Strittmatter, M.D., PH.D., the Vincent Coates Professor of Neurology and professor of neurobiology, is one of six scientists to receive the Senator Jacob Javits Award in the Neurosciences from the National Institute of Neurological Disorders and Stroke. Strittmatter's award will allow him to further study signaling pathways and loss of function studies in animal models of disease.

Edward M. Uchio, M.D., assistant professor of surgery (urology), received the 2005 Dennis W. Jahnigen Career Development Scholars Award. The two-year career development awards allow junior faculty to begin a career in the geriatric aspects of their discipline.

Raymond Yesner, M.D., professor emeritus and senior research scientist in pathology, received the Gold Medal from the United States and Canadian Academy of Pathology in May, one of the most prestigious awards in the field of pathology.

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A call to professionalism

As 100 new medical students begin their education, a physician defines the principles of their calling.

At the beginning of the White Coat Ceremony in August, Dean Robert J. Alpern, M.D., assured the 100 members of the Class of 2009 that they were where they belong. "The admissions committee did not make any careless errors in admitting you to our medical school," he told the crowd in Harkness Auditorium. "If we do our jobs, and you do yours, years from

now students will walk these halls wondering if they belong in the same institution as the Class of 2009."

Before they received their white coats, keynote speaker David L. Coleman, M.D., HS '80, professor and interim chair of medicine, noted that the ceremony started in this country in 1993 as an effort to "acknowledge the professional ideals that are the essence of being a physician.

"Professionalism," Coleman continued, "drives how we live, how we aspire and how we learn. ... I have come to believe that it is the inseparable weaving of scientific discipline with humanism that is at the core of

professionalism. We cannot and will not be humane physicians without employing science. And we cannot and will not be medically competent physicians without employing humanism."

The principles of professionalism rest on the pillars of nonmalevolence, beneficence, patient autonomy, justice, inquisitiveness, competence and teaching, Coleman said. They require, among other things, that physicians do no harm, advocate on behalf of patients rather than themselves, strive to do good, respect decisions made by patients and seek equity and justice in the delivery of care. "It should deeply



David Coleman, Nancy Angoff, Herbert Chase and James Jamieson were among the faculty helping students with their white coats.



Forrester Lee, assistant dean for multicultural affairs, welcomed Caleb Korngold to Yale.



Hasani Baharanyi donned his white coat for the first time.

BELOW Back row, Fabienne Meier-Abt, Katherine Uyhagi, Ellen Vollmer, Martin Dominguez and Corey Frucht; front row, Maya Kotas, Rachel Rosenstein, Julie Xanthopoulos and Sara Crager.



bother everyone in this room that 48 million Americans are without some form of health insurance," he said.

In concluding, Coleman cautioned the students to prepare to make sacrifices. "Medicine will require a great deal from each of you, and very importantly, it will give back a great deal to each of you," he said. "If you can find your balance while fulfilling the ideals of professionalism, you will attain the immeasurable and enduring rewards that your new profession offers. I hope your white coat will always inspire your aspirations and your ideals, from this day forward."

—John Curtis



John Forrest helped Rebecca Bruccoleri on with her white coat.



Dean Robert Alpern welcomed Michelle Collins to the medical school.

TERRY DAGRADI (7)



Titilope Oduyebo after group portraits outside the Sterling Hall of Medicine.

Reunion 2005

Alumni see the artistic side of surgeons, hear a talk on terrorism and, as ever, catch up and relive old times.

Photographs by Terry Dagradi and John Curtis



Surgeon-artists James Dowaliby, John Anlyan, Ralph Greco, Bernard Siegel, Paul Barcewicz, Eiji Yanagisawa and Michael O'Brien displayed photographs, paintings and sculptures at the Surgical Society Spring Reunion in June.

Although the reunion in June officially kicks off with a Friday evening dean's reception followed by the clambake on Harkness Lawn, in recent years a Thursday evening reunion of the Yale Surgical Society has increasingly drawn alumni to New Haven a day early. This year, early birds were treated to a discussion of the surgeon as artist. Other reunion talks included a discussion of terrorism by a psychiatrist who has worked with the Central Intelligence Agency (CIA) and a panel on advances in treatment of pediatric diseases. This year's reunion also saw the election of a new president and vice president of the Association of Yale Alumni in Medicine.

At the New Haven Lawn Club on Friday, public health alumni heard a panel on the impact of genomics on their profession and, over lunch, a keynote talk on the potential for genetics and biotechnology to improve the lives of the poor.

From surgeons to artists

As an adult Bernard S. Siegel, M.D., HS '61, returned to a boyhood hobby that had given him great pleasure. Painting, he said, is "a way of relieving the pressures of being a physician. It makes me lose track of time. I think it is the healthiest state I can be in." Siegel, whose paintings of his family and a self-portrait in surgical scrubs were on display in the Cushing/Whitney Medical Library in June, was one of three speakers on "The Surgeon as Artist," the theme of the 10th Annual Yale Surgical Society Spring Reunion in June.

Joining him in the discussion in Harkness Auditorium were surgeon

Dean Robert Alpern outlined the state of the school and plans for its future at the annual meeting of the alumni association.



and photographer James M. Dowaliby, M.D. '67, HS '72, associate clinical professor of surgery (otolaryngology), and surgeon and sculptor Ralph S. Greco, M.D. '68, HS '73, the Johnson & Johnson Distinguished Professor and chief of general surgery at the Stanford University School of Medicine.

Dowaliby has been taking pictures for 52 years. With his digital camera he documents family events and vacations and records his surgeries, but his personal and professional lives merged in this exhibit with two photographs of his sister-in-law as she prepared for radiotherapy to treat cancer. Dowaliby photographed her face as it was being fitted with a mask. He converted his color pictures to black and white, then increased the contrast to obtain stark, almost surreal images.

Unlike the other speakers, Greco—a professional sculptor for more than a decade, with gallery shows and sculptures in private collections around the country—said he has failed to find a link between surgery and his art. “I have searched in vain to find a connection that makes any sense to me between surgery and sculpture,” he said. “Surgery is about the pursuit of technical perfection, sculpture about the pursuit of beauty. Perhaps what they have in common is that in both, as we learn, we come under the influence of masters who influence us in many ways, some of which are not easily recognized.” Greco’s representational and abstract stone sculptures were among the photographs, paintings and sculptures by nine surgeon-artists on display at the symposium.

Other works on display by Yale surgeon-artists included those of John

A. Anlyan, M.D. '45; Paul A. Barcewicz, M.D., assistant clinical professor of surgery (gastroenterology); Wayne O. Southwick, M.D., former chair of orthopaedics; Michael O'Brien, M.D., PH.D., assistant clinical professor of surgery (gastroenterology); Eiji Yanagisawa, M.D., HS '59, clinical professor of surgery (otolaryngology); and Ken Yanagisawa, M.D., HS '93, assistant clinical professor of surgery (otolaryngology).

Of tyrants and terrorists

Reunion activities started off Friday with a sobering presentation by psychiatrist and terrorism expert Jerrold M. Post, M.D. '60, who has profiled terrorists and tyrants for the CIA. Terrorists, he said, tend to be “normal individuals” who have more in common with urban gang members or mobsters than with crazed fanatics. Indeed, terrorist groups screen out emotionally unstable individuals because they represent a security risk.

“You can’t explain terrorism on the level of individual psychology,” said Post, director of the political psychology program at the George Washington University and founder of the CIA’s Center for the Analysis of Personality and Political Behavior. The attractions of joining a terrorist group, he said, are rooted in collective psychology—alienated youth join to find purpose in their lives and they subordinate their individuality to the group cause as articulated by a destructive, charismatic leader such as Osama bin Laden. Group psychology binds the members together, and group and organizational psychology can push them to risky and destructive behavior, as they recognize that dissent leads to expulsion or death.



Jerrold Post discussed the psychology of terrorism, noting that terrorists are rarely crazed fanatics.



TOP Jocelyn Malkin was elected vice president of the alumni association and Frank Lobo was elected president. Donald Moore (center) is past president.

MIDDLE Donald Moore, with his wife, Christine, and daughter, Crystal, ended his term as president of the Association of Yale Alumni in Medicine this year and was honored with the Distinguished Alumni Service Award.

BOTTOM Sherwin Nuland also received the Distinguished Alumni Service Award, for his outstanding dual careers as a surgeon and author.

Religious terrorists are spurred by an ideology of hate toward nonbelievers. Although their war on modern influences depends on modern technology, technology is not the key to fighting terrorism, said Post. He proposed a program of strategic communication designed to inhibit potential terrorists from joining the group, produce dissent in the group, facilitate exit from the group and reduce support for the group. But as he showed the photo of a 1-year-old child wearing the bomb-draped vest of a suicide bomber, he cautioned that the so-called war on terror will be decades long. "We have already lost a generation," he said. "Hatred and the attractions of martyrdom have been bred in the bone from childhood on."

The state of the school

After Post's talk, alumni moved up the street to the dean's reception in the Historical Library, followed by the clambake on Harkness Lawn.

The next morning the Association of Yale Alumni in Medicine (AYAM) elected Francis M. Lobo, M.D. '92, to a two-year term as president. Jocelyn S. Malkin, M.D. '52, HS '54, FW '60, was elected vice president. Christine A. Walsh, M.D. '73, elected two years ago to a three-year term as secretary, will continue in that position for another year.

Lobo said he is assuming the presidency at a moment of "tremendous excitement. ... The School of Medicine is seeing a vigorous expansion of the missions of research and patient care, as well as a very appropriate sensitivity to the special nature of our educational mission by Dean Robert Alpern. That will be a very exciting message to bring to the alumni," he said.

Malkin, who is in private practice as a psychiatrist in Maryland, said, "I am particularly interested in the issue of women faculty, promoting equal working conditions and salaries for women." Malkin has served on the AYAM executive committee and as a delegate and member of the board of governors of the Association of Yale Alumni.

Outgoing AYAM president Donald E. Moore, M.D. '81, M.P.H. '81, and Sherwin B. Nuland, M.D. '55, HS '61, each received the Distinguished Alumni Service Award at the Saturday morning business meeting. Moore was honored for his service to his community in Brooklyn, N.Y., where he has a private practice and makes house calls. "You have always put the patient first," read his citation, which also took note of his teaching of medicine and his leadership in "embracing the cultural diversity that is a vital part of our school's—and our nation's—growth."

Nuland was honored for his "distinguished and outstanding" career as a surgeon, and for his second career as a scholar, writer and lecturer in the history of medicine. His citation noted his humanitarianism as well. "When the Asian world was devastated by a tsunami, you immediately joined a Yale medical team to travel to Sri Lanka."

Following the awards, Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, discussed the state of the school, which he described as one of advancement and expansion. A strategic planning process begun last year has created new venues for communication and identified areas for allocation of resources. "The school cannot and should not invest in every conceivable

area," Alpern said. "The areas in which it does invest should be truly excellent and among the best in the nation." Areas targeted for investment include faculty, new research and clinical programs, facilities, new research buildings, innovative medical education programs and student financial aid.

Childhood diseases grow up

Earlier that morning, at the annual scientific symposium, alumni heard from a panel of Yale researchers who are helping to rein in diseases that, in the not-too-distant past, presented parents with their worst possible nightmare: burying a young child.

Certain congenital heart defects, type 1 diabetes and cancer were often associated with poor outcomes, but "the tide is turning on those diseases," said Margaret K. Hostetter, M.D., the Jean McLean Wallace Professor of Pediatrics, chair of pediatrics, and moderator of the symposium *From Embryo to Young Adult: New Frontiers in Pediatrics*. Three Yale faculty members described their research.

Martina Brueckner, M.D., FW '90, is literally shining a light on the genetic roots of atrial isomerism—a condition in which the heart develops as a mirror image of its normal self. A team led by Brueckner, an associate professor of pediatrics (cardiology), discovered in mice that a "molecular motor" gene called left-right dynein, mapped in 1997, is crucial to a developing embryo's "biological handedness," the ability to tell left from right.

The process starts early. "By 56 days of human development, the heart is fully formed," Brueckner said. "Handedness" is determined as early

as 20 days, and if it doesn't happen correctly it "can lead to a very, very malformed heart." By examining embryos under special lighting in a microscope, Brueckner's team discovered that the cells of the nodes (organizing centers) have hair-like structures called cilia that move fluid around the embryo leftwards, leading to asymmetric development of the heart. This doesn't happen in embryos with the mutated form of dynein.

While only one in 8,500 people is born with inverted organs—and many live a healthy life without ever knowing of the inversion—the condition strikes one in 25 of Brueckner's congenital heart patients. "They're what we call our frequent flyers," she said. "They keep coming back."

The progress against type 1 diabetes has come in several large waves—the discovery of insulin in the 1920s and the advent of glucose self-monitoring in the 1970s—rather than incrementally. The next wave is the development of an artificial pancreas, which Stuart A. Weinzimer, M.D., an associate professor of pediatrics (endocrinology), called "our best shot" at diabetes management.

Researchers have two of the three elements needed, Weinzimer said. One is the insulin pump, developed at Yale in the 1970s, which is now portable enough (once the size and weight of a laptop computer, it is now no larger than a pager) to be in widespread use. A 2002 Yale study of the latest devices found that they cut episodes of hypoglycemia in half.

The second innovation is the round-the-clock glucose monitor. Some models can read blood sugar levels



TOP At the Saturday morning scientific symposium, Margaret Hostetter, chair of pediatrics, moderated a discussion of advances in the treatment of childhood diseases.

MIDDLE Martina Brueckner described her research into atrial isomerism, a condition in which the heart develops as a mirror image of its normal self.

BOTTOM Nina Kadan-Lottick directs a clinic that helps families deal with life after cancer. Many survivors of childhood cancer face health and psychological problems.

without puncturing the skin, and others sound an alarm when levels are abnormally high or low. While “we have a lot of work to do on these,” Weinzimer said—they still don’t give a completely accurate picture over a 24-hour period—“there is a place for them.” The third component to creating an artificial pancreas, under study at Yale, uses a computer that gets the insulin pump and glucose monitor “to talk to one another,” signaling the insulin pump to respond to a patient’s individual needs. “We’re getting closer and closer,” he said.

In 1997, one in 640 Americans was a survivor of childhood cancer, and that rate is expected to rise to one in 250 in five years. The progress is such that doctors face a task their peers could only dream of a generation ago—coping with problems faced by an ever-growing pool of childhood cancer survivors. “This is a growing population,” said Nina S. Kadan-Lottick, M.D., an associate research scientist in pediatrics (hematology/oncology), but “there are costs.” Many survivors have problems with growth and fertility, don’t do well in school, have self-image problems, suffer from neurocognitive impairment, develop subsequent malignancies and live shorter lives. To help the survivors of childhood cancer, especially those recovering from leukemia, Kadan-Lottick directs the HEROS clinic, a unique clinical program within the section of pediatric hematology/oncology at Yale.

Kadan-Lottick said her team is looking at the role of family strains, mechanisms of coping with life after cancer and what types of chemotherapy are more likely to lead to other medical problems later.

“There are many opportunities for screening and intervention,” she said. On the bright side, “cure is the rule, not the exception, for children with cancer.”

Public health and the human genome

“Race is really a social phenomenon, not a biological one,” said Kenneth K. Kidd, PH.D., professor of genetics, psychiatry and biology at Yale, the keynote speaker at alumni day at the School of Public Health, held at the Lawn Club on Friday, June 3. His speech kicked off a discussion of genomics and public health, an area in which health practitioners are still feeling their way.

Citing studies of 42 genetically diverse populations from around the world, from the Mbuti of Africa to the Yakut of Siberia, he said that despite obvious, skin-deep differences, the genetic diversity found within any given human population far outweighs the diversity between populations. Nearly all potential genetic variations are found in every population. “It’s really impossible to define a boundary of a race based on these differences,” he said.

Panelists at this year’s public health reunion explored how the genomic revolution might be applied to epidemiology, while cautioning against over-emphasizing genetic causes of disease and neglecting environmental and behavioral causes. At least two speakers said the promise of genomics has been “oversold” to the public. As Kidd stressed in his talk, there is still much to learn about human genetic variations.

The 400 or so variants he has studied represent a tiny, “Eurocentric” fraction of the estimated 6 million in the human genome. “We need to know how much variation there really is and

how it is distributed around the world,” he said, before genomic data can be used to relate human diversity to public health problems. As an example, he cited a study that appeared to link variants in the dopamine transporter to smoking in the United States population. But when he looked at the same gene in populations around the world, he found much more variation among the populations, irrespective of smoking, that called the original results into question.

Despite such caveats, public health professionals will be in the forefront of using genomic data, noted panel moderator Paul A. Locke, M.P.H. ’80, J.D., DR.PH., a visiting scholar at Johns Hopkins. Five panelists described how genomics is already affecting their piece of the public health puzzle.

Alan Goldberg, PH.D., director of the Center for Alternatives to Animal Testing at Johns Hopkins, said genomics will eventually allow toxicologists to use fewer animals in tests. Genomics, he said, will lead to *in vitro* replacements “that are both good science and allow humaneness.”

Lloyd M. Mueller, PH.D. ’84, an epidemiologist at the Connecticut Department of Public Health, noted that genomics’ impact on policy is “promising, but challenging to translate.” And, he cautioned, this promise is oversold to the public. For example, said Mueller, the Connecticut Legislature recently mandated an expanded battery of newborn screening tests, some of which have not been systematically studied and yield test results that do not lead to specific treatment decisions. Audience members worried about the potential legal and ethical ramifications of tests

with still-unknown false-positive and false-negative rates that are designed to detect diseases for which there are no known interventions.

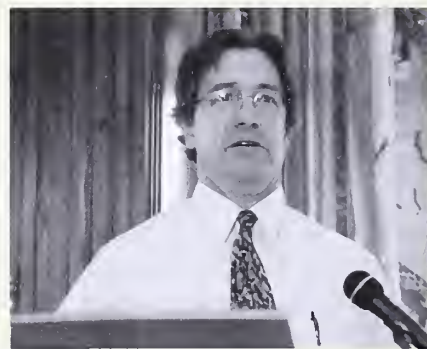
Herbert Yu, M.D., PH.D., associate professor of epidemiology and director of Molecular Epidemiology Shared Resource at Yale Cancer Center, discussed the effects of heredity, lifestyle and environment on DNA methylation, a process involved in gene expression. Disruptions in methylation can cause disease, and Yu noted that methylation patterns can be inherited but can also be changed by environment, lifestyle and exposure to chemicals.

This interplay of behavior, environment and genetic luck was also addressed by Marta Gwinn, M.D., M.P.H., the director for science at the Office of Genomics and Disease Prevention at the Centers for Disease Control and Prevention, and Kathleen R. Merikangas, PH.D., senior investigator and chief of the Section on Developmental Genetic Epidemiology at the National Institute of Mental Health and a research affiliate in epidemiology at the School of Public Health, where she was a professor until 2003. The underlying heterogeneity in populations will allow doctors to distinguish between hereditary and sporadic cases of cancers or other diseases, and to identify subgroups that are more susceptible to environmental risk factors. "Risk factors coupled with genetics and biology become meaningful," said Merikangas.

She went on to add, however, that "genomics has been grossly oversold." Discoveries such as the putative "gene for smoking," she said, could make people feel they are absolved from



Keynote speaker Kenneth Kidd said genetic differences do not define race, which is a social rather than a biological construct.



Panelists discussing the implications of genomics for public health included, clockwise from top left, Kathleen Merikangas, Alan Goldberg, Lloyd Mueller and Herbert Yu.

In his luncheon address Peter Singer argued that genetics and biotechnology can improve the lives of the poor.



responsibility for their high-risk behaviors. "We need to help people understand and not overinterpret the role of genes," she said.

Past progress, future challenges

At the public health alumni day luncheon, Interim Dean Brian P. Leaderer, M.P.H. '71, PH.D. '75, began by praising his predecessor, Michael H. Merson, M.D., the Anna M.R. Lauder Professor of Public Health, who stepped down in December after 10 years as the first dean of public health at Yale. "I think it is really important to all of us as graduates to acknowledge what he has done," Leaderer said, citing a twofold increase in the size of the faculty, improved facilities, increased visibility for the school and the creation of the Center for Interdisciplinary Research on AIDS.

As the search continues for a new dean, however, a report from the provost's office has noted some areas for improvement. The report called for continuing a strong focus on research, an improved educational program and an examination of administrative structure, Leaderer said. And, the report said, the school lacks a critical mass. "We are too small and we lack the money and infrastructure to grow," Leaderer said. The subtext to this discussion, he added, was independence. EPH, which is accredited as a school of public health, has long sought to be free-standing, rather than a department of the medical school. "The university's response was that there will be no independence in the foreseeable future."

In response to the provost's report, the school has begun a strategic planning process. "We are paying more

attention to the quality of our teaching," Leaderer said. The school is also planning a one-year master's program for those with a degree in health-related science. And a new program with Yale College would create a joint five-year program in which undergraduates could major in public health and after graduation spend another year obtaining an M.P.H.

Jerald A. Fagliano, PH.D., M.P.H. '85, was inducted into the Alumni Public Service Honor Roll for his service to Vermont and New Jersey in the area of environmental health. David A. Newman, M.P.H. '96, received the Eric W. Mood Alumni Award, established in 2005 to recognize an alumnus or alumna demonstrating outstanding promise as a new professional in public health. As corporate director of environment, health and safety at Millipore, a bioscience company headquartered in Billerica, Mass., he developed, implemented and evaluated programs for the company. James S. Marks, M.D., M.P.H. '80, the senior vice president and director of the health group at the Robert Wood Johnson Foundation, received the Distinguished Alumni Service Award. He was previously in a top leadership post at the Centers for Disease Control and Prevention.

Marks said people often miss the connection between public health and their daily lives. "We have to make that connection—that screenings, getting your flu shot are connected to living the kind of life you want," he said.

"... those other 5 billion people ..."

After lunch, Peter A. Singer, M.D., M.P.H. '90, the Sun Life Financial Chair in Bioethics and director of the Joint

Centre for Bioethics at the University of Toronto, received the 2005 Award for Excellence. He began his remarks by pointing out the difference in life expectancy in the United States and sub-Saharan Africa. "Eighty years and rising and 40 years and falling. If that isn't the mother of all ethical challenges, what is?" he asked, before pondering how technology and genomics can improve global health. Showing a slide of children in a coastal village in India, he said, "They are all barefoot and they live in thatched houses. ... Right in the middle of their village is an information kiosk where they can access the Internet." The point, he continued, is "the potential of science and technology and innovation to better the lives of the poor. I want to argue that genetics and biotechnology have comparable, if not greater, potential."

As an example he pointed to "the largest mass poisoning in world history" in Bangladesh, where 50 million people are affected by exposure to arsenic in drinking water. At the bottom of the country's wells are bacteria responsible for the arsenic, he said. But in Australia there are bacteria that remove arsenic from water. Genomics, Singer said, has the potential to solve the problem in Bangladesh. Sequencing the genomes of these two bacteria could yield a way to offer a solution to the problem, he said.

"We need to keep the focus on those other 5 billion people in the world, those that have half the life expectancy of people in this room," Singer concluded.

1945

60th reunion

Although time and tide and the vagaries of advancing years have diminished the numbers and vigor of this class, we had a splendid turnout, attracting more attendees than some classes junior to us.

Making the trip to New Haven were **John** and **Betty Anlyan** (basking in the glory of the greatest gift ever to the School of Medicine), **Dick** and **Verne Breck** (appropriately enjoying the reunion they orchestrated), **Sandy Cockerell** (with son Dr. Charles and lovely history professor daughter-in-law Karen), **Dick Dyer** (white-haired but otherwise unchanged since his glory days), **Sid Feuerstein** (looking tanned and terrific), **Ray** and **Pat Gagliardi** (still the prettiest girl who found her husband in the air raid shelter in the library), **Bill** and **Marj Jenney** (he is the dignified and impressive doctor type), **Lee** and **Barbara Jones** (no one had a more gorgeous caregiver than Barb), **Mike** and **Geri Lau** (upbeat and optimistic and just plain fun), **Charlie** and **Laura McLean** (with daughter Patti, who has inherited the best from both—**Charlie** introduced me to my life-long addiction to golf). Our best surprise was **Gove Hambidge**, who was attending his first-ever reunion and had a great time. **Gove** still practices psychiatry full time in Golden Valley, Minn.

We shared the spectacular clambake dinner and sherry lunch; we toured the magnificent Anlyan Center and felt vicariously the pleasure that the donor was one of us; we took a tour of historic New Haven and heard some really informative lectures. Possibly the best was hearing from the new dean. He seems to be the right man in the right job at the right time. The city, the university and the medical school campus have made tremendous strides since last reunion. The future looks great.

Far and away the best of all, however, was the warm cama-

raderie of our group. It was almost as if it was June 1942, and we were young again. Our next reunion will be in 2010 and **Gove** has already committed to come. I hope the rest will do the same.

Ray Gagliardi

1955

50th reunion

There are by our last count 60 living members of our class. A total of 30 were able to attend the reunion for at least one day, and most for three days. **Leo Cardillo**, who is still in practice, was able to come for only a short time on Friday, but his presence brought our total attendance to 50 percent. **Alan Stone** was only able to come for Saturday, but also was a welcome face. (He still looks like he did 50 years ago.)

The committee had made a number of phone calls to members who had not responded to the initial letters. It was really nice to talk to them, but unfortunately the reasons for not coming were usually because of illness of the classmate or spouse. Some were quite ill, but as physicians, we would expect this in a group of people in their 70s. What was encouraging was the general overall health of our group. Almost everyone is retired and finding many interesting and productive pursuits to keep them busy.

The week after the reunion, I went to Atlanta for another event, and was able to have lunch with **Roger Lester**, who could not come to the reunion because of another commitment. He is doing some scholarly work in history and philosophy, and was giving some lectures the weekend of the reunion. He will be at the 55th.

Again, one of our classmates was honored; **Shep Nuland** received the Distinguished Alumni Service Award. As usual, he was gracious and articulate in his acceptance speech.

We were fortunate in having our oldest classmate, **Pat Costa**,

attending as well as our youngest, **Guy McKhann**. **Harry Kendall** and **Sandy Zuckerbraun** traveled from distant California with Wanda and Ruth to attend. **Sandy** is still in practice and because he sees many Mexican-Americans, he has become fluent in Spanish. You see, you can teach an old horse new tricks.

Frank Johnson is retired, but still lives in the vast outreaches of Montana. **Milt Corn** was in from Bethesda, Md., where he is active in what seems like an important but somewhat confusing project at the NIH. I'm sure with his involvement it is important.

Jim Garlington is now working on a project to collect digital pictures from the reunion and also some from people who could not attend. He is going to put them on a CD and send it to all class members. I thought it was a great idea, and he is to be congratulated for this work. See you at the 55th.

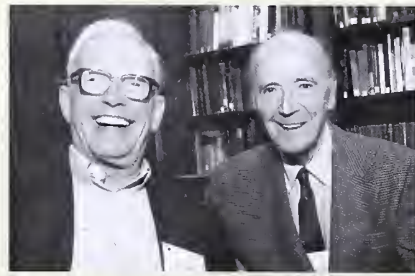
Jack Landau

1960

45th reunion

Our 45th reunion was a source of great pride for the Class of 1960, because the keynote speaker for the entire alumni body was our own **Jerry Post**. **Jerry**, a distinguished professor of psychiatry and political science at George Washington University, has written six well-received books on subjects ranging from the psychopathology of political leaders to the origin and perpetuation of terrorism. Many of us had already been familiar with his thinking not only from his books, but also from his numerous appearances on cable TV.

On Friday afternoon **Jerry** spoke eloquently and unsettlingly about the rapid propagation and intensification of terrorism. His talk, subtitled "When Hatred Is Bred Into the Bone," highlighted the bitter irony that our political leaders are confidently adopting bellicose policies that are only mak-



ing the phenomenon worse. The fact that there are no panaceas and that terrorism will be with us for generations to come was deeply troubling to the audience; this struck us as the mark of a highly successful talk.

The festivities continued into the evening. During the clam-bake, which seems to get more delicious each time, we began to unwind and renew our old friendships. There was general agreement that the finalists for the Obscenely Young Forever category were **Gerald Cimmino**, **Neil Cooper** and **Sue Kleeman**. By virtue of his continued stature as basketball star, **Lanny Ames** was charitably awarded honorable mention. Moreover, **Cooper** had lost so much weight that no one recognized him. We suspected they were all plants from the Class of 1990. However, the rest of us all looked so fit and terrific that no one really envied them, except for **Kleeman**. The Most Eloquent Award went to **Bob Wallach**, whose brave and moving reminiscences brought many of us to tears.

On Saturday we were all pleased by Dean Alpern's talk. It seemed engaged, thoughtful, serious and leaderly. We were persuaded that our school is in very good hands and will retain its outstanding rank for years to come.

But the *pièce de résistance* was, as always, the Saturday evening dinner at the Lawn Club. The tone was set by class agent **Tom Kugelman**, who reported that our class had contributed more than any other reunion class to the Annual Fund. This was due in large measure to one extremely large gift from **Eric Kindwall**, who spoke movingly of what Yale had meant to him.

And so did the rest of us. We all got up in turn and gave accounts of ourselves and our lives. One common thread was that in many different ways, even for those of us who felt we had not thrived within the Yale System and had not been happy here, the Yale experience had

somehow defined us—or more accurately, had helped us define ourselves—and helped us become what we are today. We discovered that on our first day of school each of us had been convinced that Yale had made a mistake in admitting us, and that each of us was convinced that he or she was the only one who felt that way. And over time we discovered that each of us had been wrong. That's quite a tribute to Art Ebbert and the late Tom Forbes—not to mention all the rest of our splendid faculty.

Jerry led us in observing a brief silence in honor of our deceased classmates: **Ormond Brody**, **Tom Carson**, **Stan Chung**, **Dave Dunn**, **Mal Golden**, **Irv Guttenberg**, **Arthur Martin**, **Kent Morest**, **Mike Moynihan**, **Ross Snyder**, **John St. Andre** and **Brian Welch**.

Present at this extraordinary occasion were **Vic** and **Laura Altshul**, **Lanny Ames**, **Neil** and **Teresa Cooper**, **Jon** and **Carol Courtney**, **Jim** and **Kitty Eustermann**, **Gene Gaenslen**, **Jim Gilman**, **Bill Kaden**, **Eric Kindwall**, **Sue Kleeman**, **Tom** and **Alice Kugelman**, **Tom Lau**, **Bob Marcus** and friend **Vie Simons**, **Al** and **Barbara Newcomb**, **Tom** and **Danielle Okin**, **Fred** and **Ruth Palace**, **Jerry** and **Carolyn Post**, **Nancy** and **Bill Powell**, **Buzz Robinson**, **Al Ross** and friend **Jane Semmons**, **Dan** and **Lina Rubin**, **John** and **Suzanne Schrogie**, **Bob** and **Judy Wallach**, **May** and **George Wang**, and **Ron Yankee**. Present in spirit was **Malin Dollinger**, who had intended to come before his wife, **Lenore's**, sudden illness and who sent a warm and moving account of his recent life.

Victor A. Altshul

1965

40th reunion

The Class of '65 had a wonderful 40th reunion in early June. We enjoyed the traditional shore dinner under the tent at Harkness, and a lovely dinner at the Quinnipiack Club on Saturday. Twenty classmates made it back and enjoyed catching up—some

have been regulars at reunions, others first-timers. Attendees included **Amy** and **Tom Aoki**, **John Coyle**, **Greg Culley**, **Mike** and **Susan Cummings**, **Carl** and **Emi Ellenberger**, **Chris Gates**, **Frank** and **Donna Grady**, **Gary Gross** and **Betsy Shure**, **Bob** and **Donna Gryboski**, **Reed** and **Ellie Heffner**, **Dave Hill**, **Edgar** and **Ellen Hull**, **Carl Hunt** and **Joyce Shoemaker**, **Ron Karpick**, **Mohandas** and **Joanne Kini**, **Larry** and **Linda Ossias**, **Bob** and **Mary Pickens**, and **John** and **Greta Seashore**. Five of us have retired and some have switched career paths, but most are still practicing medicine actively. Just can't keep this group down. There was considerable sentiment for having the occasional mini-reunion more frequently, especially for those of us who live relatively near each other. Perhaps we Northeasterners could gather at **Carl Ellenbergers'** Mt. Gretna (Pa.) music festival next summer. If anyone is interested, let me know (john.seashore@yale.edu). Is anyone on the West Coast up for organizing something out that way? We hope to see even more people next time around.

John Seashore

1970

35th reunion

Our class reunion dinner was held in the library of the Quinnipiack Club on Saturday evening and attended by 15 members as well as their spouses and guests. Following numerous photo shoots to accommodate late-arriving members, we enjoyed an excellent dinner and had a nice time catching up on the personal and professional lives of what was truly an eclectic class. The attendees included **Elissa** and **Dan Arons**, **John Blanton** and **Beth Balschi**, **Paul** and **Judy Braun**, **Romney** and **Mary Sue Burke**, **Anne Curtis**, **Jonathan** and **Rosanne Ecker**, **Rick** and **Ruth Edelson**, **Harvey Fernbach** and **Ann Birk**, **Tom Gouge**, **Paul** and **Patricia Hessler**, **Gerry Kennealey**, **Mark** and **Susan Korsten**, **Bob** and

Joan Rosa, **Joellen Werne**, and **Karl** and **Diane Wustrack**, as well as special guest **Rose Papac**. **Rose**, one of the outstanding educators and clinicians from the classical era of Yale medical school, announced that she will be retiring this July and plans to concentrate her efforts on writing, including a book. All of her many grateful students wish her well. I will be sending out a composite of e-mails I have received that provides specific information about many members of our class. If you do not receive this communication and wish to obtain it, please contact me (rrosa@northwestern.edu).

Bob Rosa

1975

30th reunion

Once again, it was quality, not quantity in attendance, that had us all having a good time at new New Haven restaurant L'Orcio for our Saturday dinner. **Liz Gawron** and **Paul Johnson** came all the way from California. **Paul** is an expert diver and scuba instructor as well as an underwater photographer. **Brendan Clifford**, too, came in from the California beaches, noting he has retired from his surgical career—he will be spending some time this fall with his wife in Massachusetts. **Dawn Hassinger** came up from Atlanta. **Dawn** spends her time doing medical writing these days. **Vivian Reznik** spent several days visiting with me. Besides doing academic pediatrics at the University of California-San Diego, she is researching a book on the beginnings of coeducation at Yale. **Vivian** and I were especially upset that **Barbara Stoll**, who has just been named chair of peds at Emory, didn't make it up for the event—we were hoping we could cause just as much trouble as we used to. The more local contingent was **Mark** and **Sharon Ruchman**, coming down from Washington, Conn. **Mark** is a very active ophthalmologist in Waterbury. And **Frank Watkins**, who is an

orthopaedic surgeon, came up from New Rochelle, and even though his lovely wife is a lawyer, we all had a good time. I have just recently given up obstetrics, only because of the malpractice insurance—and I spend the time I should be delivering babies harassing as many politicians as I possibly can.

We did receive some “regrets” with information. **Hymie Milstein** is still happily practicing internal medicine at Kaiser in LA—one suggestion is that we should hold a reunion out there, with so many classmates there. **Kathy Shepard** is taking time off from pediatrics to spend the year in Italy with her husband, the newly retired dean of the Law School at Duquesne University. And **George Noble** was busy at many family graduations around central Iowa, where he is busy doing peds surgery. **Sid Spiesel**’s peds practice in New Haven is still very busy, but he couldn’t come to the reunion because his family held a 65th birthday party for him that evening.

However, what I found most gratifying at the reunion was seeing our professors—folks like Dr. Braverman and Dr. Kushlan—having a good time, still practicing and teaching and reassuring me that we all have a lot of time left to have fun. And **Vivian** and I have a mission for the next reunion—to raise a bundle of money for the reunion fund—more on that in subsequent mailings!

Mary Jane Minkin

1980

25th reunion

Our 25th reunion was graced by good weather and a good crowd. Twenty-one classmates came, many with their spouses, and some with children. We enjoyed the traditional clam-bake Friday night, the sherry lunch Saturday and a wonderful class dinner at the Quinnipiac Club. The dinner was made special as each classmate shared memories and updated the

group on the events of their life over the last 25 years—it barely seems possible as most people looked very much the same.

The California contingent included **Sittiporn Bencharit** and wife Reyline. They have two children. **Sittiporn** has been happily engaged in a private GI practice for 18 years. He says, “Keep in touch, be here at the 50th and support the medical school.”

Cesar Molina, irrepressible as ever, came with wife Linda from Los Altos. He has a satisfying career as a cardiologist and still meditates. He was eager to show photos of his two daughters. Of special note, **Cesar** has a winery for sale and he provided samples of his award-winning wine at the class dinner. **Nancy Todes Taylor** is assistant chief of dermatology with the Permanente Medical Group in San Rafael, Calif., where she does mostly laser, skin cancer and cosmetic dermatology. She and husband Graham have two children. She goes to Australia (where her husband comes from) “almost all the time.”

The mid-section of the country was represented by **Walter Williams**, who is a professor of radiology at University of Arizona Medical School. **Walter** had the honor of seeing one of his two sons, Steven Williams, M.D. ’98, finish this year as chief resident in plastic surgery at Yale. **Walter** also reports that he has a serious hobby as an amateur radio operator. **Craig Brooks** passed through at the class dinner and recounted some of his adventures working as an ER physician for Aramco in Saudi Arabia for the last 12 years. **Craig**, his wife, Agneta, and their two children are moving to Colorado (someone has to keep those ski slopes busy!).

From Miami came **Eddie Alfonso**, one of our stalwart class agents, and wife Molly along with one of their children, Eduardo. **Eddie** is busy as a professor at the Bascom Palmer Eye Institute. **Eddie** and Molly have two other children, well into their 20s and engaged now in chal-

lenging careers. **Patricia Brown**, from Bethesda, Md., has experienced a number of transitions this year. “With the death of my father, I’m now a middle-aged orphan.” Another change has been taking on a new position at the FDA reviewing new medicines for dermatology, while at the same time maintaining a toehold in clinical practice.

The Big Apple contingent included **Al Siu**, who is professor and chair of geriatrics at the Mount Sinai School of Medicine. **Al** and wife Margaret have two fairly young children. **Al** proved his devotion to them by wishing them goodnight by cell phone at the Friday clambake. **Jonathan Jacobs** dropped by for the class dinner. He is professor of general internal medicine at Cornell. He and his wife, Carolyn, have two boys. **Jonathan** is proud to have been able to start a \$75 million AIDS treatment program in New York City as well as a program in Nigeria. **David Goldberg** is busy in nearby New Jersey with his skin laser and surgery practice. He and wife Rachel have four children, one of whom wants to be a doctor despite today’s challenges to the profession.

Never having left the comforts of New Haven are **Gary** and **Debbie Dyett Desir**. **Gary**, a nephrologist, is chief of medicine at the Connecticut VA Healthcare System, West Haven campus, and associate chief at Yale. **Debbie** is a rheumatologist in private practice. Together they have four children. **Gary** recalled how he met his wife while sharing an anatomy table. **Jean Bolognia** is professor of dermatology at Yale and her husband, Dennis Cooper, is also on the faculty, in oncology. Inside sources tell us **Jean** has become well-known within the specialty of dermatology for serving in a number of leadership positions and for having been the co-editor of what is becoming a popular dermatology textbook. **Ann (Henderson) Hoeffer**, social chair for this reunion and greatly appreciated, continues to be happy in her private pediatric practice. **Ann** and husband Ben





Bradburn have two daughters. **Larry Young** and wife Lynn Tanoue (M.D. '82) have three children. **Larry** is a professor of medicine in cardiology and Lynn is a pulmonologist. **Larry** states that it is special to be a part of the university community. **Barbara Fallon** and husband Bennett Bernblum live in nearby Old Lyme, Conn., and have two children. **Barbara** is in private practice in oncology and an assistant professor at the University of Connecticut. Rose Papac was **Barbara's** mentor at Yale.

Marty Silverstein, from Newton, Mass., has a continuing career with the Boston Consulting Group. He helps biotech and biopharm companies improve their product development process. He and wife Andree, a dermatologist, have two children. **Mary Hill Wise** from Rochester, N.Y., came to the reunion on Friday. She practices holistic medicine and with husband Robert has four children.

The final crew consists of three classmates who graduated in 1981 but maintain ties to the Class of 1980. **Phil Lee** and his wife, Diane, share a psychiatry practice in New York City and together have two children. **Charles Shana** is a gastroenterologist in practice for the past 15 years in Newport, R.I., and Fall River, Mass. He and wife Miriam have two sons. **Donald Moore**, wife Christine and daughters were present at many reunion events. **Donald** practices internal medicine and is on the faculty at Cornell. **Donald** also is past president of the Association of Yale Alumni in Medicine and was honored to receive the Distinguished Alumni Service Award.

OK, you laggards out there: you missed a good time (and some really fine wine). The 30th is only five years away, so mark your calendars now. See you all there.

Patricia Brown

1985

20th reunion

Returning members of the Class of 1985 gathered for dinner at

the home of pediatrician **JoAnne Burger**. While the reunion dinner was scheduled for Saturday, **Brian Lombardo** (ever the eager beaver) got a jump on his classmates by showing up on Friday night. **Brian** is doing general practice in southern Vermont, having recently returned with his family from an extraordinary sabbatical experience during which he worked at a hospital in Kigali, Rwanda. Saturday's festivities reunited another dozen or so classmates, including ophthalmologist **Kimball Woodward**, who is practicing in Middletown, N.Y., and pediatrician **Fred Santoro**, whose practice is based in East Lyme, Conn. The passage of time has not altered **Fred's** trademark laugh. Pediatric endocrinologist **Jon Nakamoto** has joined Quest Diagnostics. He and his family came in from the West Coast for a week of med school and college reunions.

Jonathan Lewin has moved from Cleveland to Baltimore to assume the chairmanship of the Johns Hopkins department of diagnostic imaging, a position only recently vacated by the current director of the NIH. **Gail Mattson-Gates** is a plastic and reconstructive surgeon in Los Angeles, and she strenuously denies participating in any Hollywood extreme makeovers. **Sam Goos** is also plying the skin trade as a dermatologist, with a growing multisite practice in the Boston area. The Boston contingent included **Guy Fish**, who is working in venture capital, and **Sue Korrick**, who is on the faculty at Harvard and focusing her efforts on occupational medicine and exposure to environmental toxins. Prolific author **Bob Klitzman** is on the psychiatry and bioethics faculty at Columbia. He has written several books and has participated in television documentaries. **Jackie Gutmann**, who is a fertility specialist in Philadelphia, blew out of a bar mitzvah before the waiters brought in the flaming desserts and raced to Connecticut in time to join the gathering. **JoAnne** was very gratified to

have her entire anatomy four-some reunited (although the group's cadaver was otherwise engaged). The group included ENT **Barb Guillelte**, who came down from Providence, and rheumatologist **Paula Rackoff**, who came up from Manhattan. Completing the anatomy quartet was **Jeff Lowell**, who has acquired a fascinating skill set. In addition to serving on the faculty of Washington University in St. Louis as a liver and kidney transplant surgeon, **Jeff** has been trained by the St. Louis police as a hostage negotiator and spent time working on disaster planning for the Department of Homeland Security. Harrison Ford has expressed interest in portraying **Jeff** when filming begins on the movie version of his life. The evening ended with the general agreement that the entire class still looks fabulous, is a lot of fun to be around and should get together more often.

JoAnne Burger

1990

15th reunion

Some people may feel that the 15th reunion wasn't worth attending, but those of us who made it had a good time. It was my first time seeing my classmates and my first time back to New Haven since graduation, and much has changed. I couldn't believe that Grand Central had changed to a Walgreen's and Barnes and Noble bought out the Yale Co-op.

I also had a chance to tour the new Anlyan Center—home to the new anatomy lab and one of the largest buildings on the Yale campus. It is second only to the Payne Whitney gym in size and holds educational space as well as research labs.

Fortunately, none of our classmates have changed much! I caught up with **Nancy Angoff** and her husband, Ron, early on. As you all know, she is now the associate dean for student affairs for the medical school—but for us, she's still known as

"mom." **Will Andrews** made it from Boston with his family. **Will** still spends time with his private practice, but I believe he spends more time as senior medical director of Sepracor.

Chandler Samy came up from Ocala, Fla., with his family. He is a retinal surgeon in private practice. **Jonathan Foster**, an ob/gyn in Waterbury, came in with his wife and parents. His father was present for his 50th reunion.

New York was well-represented at our class dinner on Saturday. **Sam Colin** came in with his wife. He spends much of his time managing a health care investment fund with First Manhattan Co. **Ethan Halm** also made it. He is the chair of medicine at Mount Sinai. Finally, **Julia Schillinger** also drove up from New York. She is director of surveillance, epidemiology and research at the New York City Department of Health and Mental Hygiene, Bureau of Sexually Transmitted Disease Control. Her business card is the size of a postcard!

Robin Hornung probably wins the award for the longest trek to be with us. She came from Seattle by herself—but brought plenty of pictures of her son and husband. She is the head of pediatric dermatology at the University of Washington. **Ercem Atillasoy** (he'll always be known as **Tilly** to us) came from Philadelphia. **Tilly** is a dermatologist and the director of internal medicine, dermatology and tissue engineering at Novartis Pharmaceuticals Corp. We also had a chance to catch up with **Jennifer Mark**, who came in for the dinner. She's been busy in an ER in New England (I can't remember just where—a good reason for me to make it to the 20th).

Finally, I came in by myself from Concord, N. C. There, I am an electrophysiologist with a group of eight other cardiologists at a moderate sized community hospital. I am married to Jane Rasmussen (Class of '89) and have twin 9-year-old daughters!

Overall, all had fun, but the evening did have a bit of a sad note. **Dan Stryer** passed away from a brain tumor this spring. He really had wanted to make the reunion, which filled us all with a certain sadness. We all decided that we wanted to do something meaningful in his name. I believe **Nancy** and **Tilly** are going to come up with some ideas. We need to move on this to make it really meaningful. Stay tuned for more information about this later.

Well, that's it. I hope to see more of you at the 20th reunion!

Tom Christopher

1995

10th reunion

I am glad to report a strong turnout for the Class of 1995. It was wonderful, considering how busy we all are with our careers and families. **Chris Lykins** traveled from his busy otolaryngology practice in Phoenix to share memories with his friends. **Chris** has found a great spot for all of us to visit in Arizona and invites us all to visit him at Burning Man next year. **Chris Wahl** traveled from the University of Washington in Seattle. It was really an expedition, since his five-month-old triplets accompanied him. His wife, Rebecca, deserves most of that praise. Although we are sad that **Chris** has left the Yale community, we are happy to see that he is practicing sports medicine at the very institution that he once passed on. **Emily (Rosenberg) Roth** (pediatrics) and **Jake Roth** (psychiatry) were able to join us at the clambake. They and their two children spent the past few years at Harvard. No degrees for the children thus far. They have all recently headed for warmer weather near **Todd Alamin** and **Artis Montague** in California. **David Morales**, his wife, Mary, and their two children traveled from Houston, where **Dave** is a pediatric cardiothoracic surgeon, after nine years of training. **Nick Schwartz** and his wife, Loretta, traveled from Seattle for the

occasion. **Nick** is truly remarkable for being our only alumnus to have completed two residencies. However, most of us do believe that he is best suited for psychiatry. While he did not stay at the President's mansion we understand that his quarters in New Haven were comfortable.

Jeff Algazy and his lovely wife, Abbey, came up from New Jersey for the event. **Jeff** has been doing consulting for a number of years and is happy spending time with his daughter. **Brian Adams**, **Jilda Vargus** and their daughter came back to Yale from Cincinnati. **Brian** is practicing dermatology and **Jilda** is practicing psychiatry. **Brian** and **Jilda** both exemplify the spirit of our class. Their assistance with fund-raising was appreciated by all of us. **Tim Kinkead** and his wife, Lisa, drove in from Cape Cod, where **Tim** is practicing orthopaedics. **Tim** now has a look-alike son, who fortunately has his mother's temperament.

Christine Brozowski came 3,000 miles, from Berkeley. Her knowledge of wine makes her a very useful contact when traveling to Napa. My neighbor **Jon Driscoll** came with his wife, Jenna, and their 4-month-old twins. **Jon** has a great orthopaedic practice in Connecticut. He is even operating on fellow alumni! It was great to see **Margi Rosenthal** in attendance. Although difficult events brought her back to New Haven, we are glad to see her practicing pediatrics at Yale. **Chip Skowron** and his wife, Cheryl, came in from Greenwich to catch up with old friends. **Chip** is happily running a successful hedge fund, and has three children. As for myself, I am living on a farm with my wife, Holly, and our two children. I also practice pediatrics on the side.

It was really wonderful seeing everyone back at Yale. It was inspiring to see how far people traveled—particularly with kids! I am looking forward to seeing more of us back in the coming years. **Barbara Garcia**, **Alice Chang**, **Ben LeBlanc**, **Erin LeBlanc**, **Eric Hughes**, **Larry Solomon**, **Tim Hong**,



Dorothy Novick and **Eric Gomes** all regret not being able to make it this time. We certainly have an exceptional class. I look forward to many memorable reunions to come.

Steven Craig

2000

5th reunion

The Class of 2000 turned out in good numbers for our first reunion, with slightly under 20 percent of the class in attendance. While most attendees were from the Northeast, we had a few long-distance travelers as well. Not too bad considering many are still in training. The weekend offered fine weather for the traditional New England clambake on Harkness Lawn, and a spectacular dinner hosted by the 50th reunion class at the Graduate Club. Our class has embarked on a wide range of paths since leaving Yale five years ago.

Jen Dorosz was on an East Coast swing, having finished her first year of cardiology fellowship at the University of Michigan. She spent an extra year in Seattle as chief resident at the University of Washington. **Arvind Venkat** is now an emergency medicine attending at the University of Pittsburgh. He was accompanied by his wife, Veena, who is finishing a pediatric GI fellowship, and their 6-month-old daughter. **Jonathan Erulkar** was recently married to Dierdre Carrol (YVN '00) and is now completing his orthopaedic training. Next year he will join the Boston crowd as he pursues a spine fellowship at New England Baptist.

The New Haven residents were well-represented. **Oscar Colegio** has finished a preliminary year in internal medicine at YNHH and will go on to train in dermatology at Yale next year. He is married to Stephanie Colegio-Eisenbarth, who will be going on to a residency in laboratory medicine. **Dan Negoianu** has completed his chief residency year at YNHH and will leave the Elm City for a nephrol-

ogy fellowship at the University of Pennsylvania. **Michelle Mak** and her husband came to the clambake with their beautiful baby; **Michelle** is practicing dermatology in Bridgeport. **Andrew White** is finishing his orthopaedic training, with plans to start a spine fellowship in July. **John Mahoney** braved the weekend with his wife and their infant son Jack, all before driving across the country to start a hand surgery fellowship in California.

Joanna Sheinfeld and her husband, Mark Paltrowitz, are the proud parents of Leila. **Joanna** just finished her geriatrics fellowship at Yale and will be returning to Mt. Sinai, where she was chief resident along with **Dan Jacoby**. **Dan** and his wife, Stephanie, live in New York, where **Dan** is pursuing fellowship training in cardiology at Columbia. **Joanna** will be practicing alongside **Jon Ripp** as part of Mt. Sinai's Visiting Doctors Program, which cares for homebound elderly in New York City. **Jon** and his wife, Melissa, spent a year practicing in Alaska before returning to New York.

Other New York attendees included **Keri Adelson** and David Grodberg; **Keri** is juggling a fellowship in hematology and oncology at Columbia with taking care of Paley, an adorable toddler. **Maya Salameh**, having also finished a chief residency year at YNHH, will be moving to New York to practice vascular medicine at Columbia. **Jodi** and **Elie Levine** have three daughters; **Jodi** is completing training in dermatology and **Elie** is finishing his residency in plastic surgery.

Members of the Boston contingent were distressed that they had to come to New Haven to meet up. **Amy Nuernberg**, another YNHH chief resident, is completing a fellowship in occupational health at the Harvard School of Public Health, and will go on to a fellowship in pulmonary and critical care. **John Abraham** is finishing up his residency in orthopaedic surgery, and will go on to specialize in

orthopaedic oncology. **Karin Andersson** is finishing up her clinical year in a GI fellowship at Massachusetts General Hospital (MGH); she is married to Brett Cohen, who was also in New Haven for his 10th college reunion. **Deborah Wexler** is finishing up her chief residency year at MGH before continuing her fellowship in endocrinology. Her husband, **David Friedman**, is very happy to be back in the lab after finishing his training in nephrology. **Carl Seashore** is practicing primary care pediatrics and working in the pediatric hospitalist program at MassGeneral Hospital for Children. His son, Luke, enjoyed the time with his grandparents as well as all the festivities.

There were day trips, mountain bike rides, scenic tours and even lectures spread over the weekend for all to enjoy. It was truly wonderful to catch up with so many old friends, and see how we, as well as New Haven, have all changed in five short years. We hope to see more of you at the 10th.

Deborah Wexler
Carl Seashore

PA Program

In June alumni of Yale's Physician Associate (PA) Program held their first reunion, bringing together graduates from the program's 35 years. The reunion is expected to become an annual event, said Mary L. Warner, PA-C, M.M.Sc., program director and assistant dean. "Every year we will have a dinner and invite our graduates to participate in activities throughout the medical school."

About 50 graduates renewed friendships and made new ones at the Graduate Club. Warner also described the state of the program: its accreditation was renewed last year, and thanks to a change in school policy, PA faculty now have the standing of clinician-educator track faculty. And, Warner said, an alumni outreach program is in the planning and development stages.



From Yale to Africa, an alumna finds her niche

A decade after her graduation, Rachel Bronzan studies malaria in Malawi.

On a typical morning in Malawi's rainy season, which runs from November to May and brings mosquitoes out in force, **Rachel N. Bronzan, M.D.**, '95, M.P.H., sees patients with severe malaria. "It's sort of a perverse lottery jackpot," said Bronzan of the ward she works on at Queen Elizabeth Central Hospital in the city of Blantyre. "We can provide better care because we have fewer patients, but you have to be very, very sick to come to our ward."

In the dry season, Bronzan puts on her public health hat—she works for the Centers for Disease Control and Prevention (CDC) on epidemiological studies and disease monitoring for Malawi's National Malaria Control Program.

It is in Malawi that Bronzan has combined her love of Africa with an interest in science and a desire to use medicine to help others. Malawi, in southeastern Africa, has been her home since 2002, but Bronzan's interest in Africa started long before. "When I was young I was always taken with the idea of Africa—its natural beauty, diverse indigenous cultures, exotic wildlife and vast expanses of land and sky," she said.

She first traveled to Africa in 1991 as a Downs fellow studying HIV in Senegal. During her fourth year at Yale she went to Kenya for a clinical rotation and worked at a malaria research post. Now Bronzan lives in Blantyre, the commercial and industrial center of Malawi, a landlocked country of 94,000 square kilometers of rolling plains with meandering rivers, vibrant green tea plantations and peaked highlands bounded by Mozambique, Zambia and Tanzania.

Bronzan's foray into medicine seems natural when you understand her beginnings. Her father, a theoretical particle physicist, taught at Rutgers, and her mother, a clinical social worker, counseled psychiatric inpatients. She absorbed

her father's methodical, logical approach to problem solving and her mother's nurturance and respect for others. Growing up with a younger brother only a half-mile from their maternal grandparents, she was also inspired by her grandfather, a physicist who worked on the development of color television at RCA. In his basement workshop they blew glass, built and detonated small cannons using compressed gas to fire bits of pencils and erasers, and created electromagnetic fields with wire coils (like an MRI) in which Bronzan's grandfather tested the effect on his vision.

In 1990, after graduating from Stanford with a degree in chemistry and working in an infectious disease lab, Bronzan began medical school. By her fourth year she still felt the lure of research, but during her travels in Kenya she saw the rewards of treating patients. "I was impressed by the great impact that the family physicians made, with broad training and simple interventions skillfully applied in a resource-poor setting. I realized that if I were to practice medicine I would most likely do it in a setting like that, where basic need is high," she said. She spent a fifth year at Yale, during which she got an M.P.H. at Harvard, and in 1995 began a residency in California at the Community Hospital of Santa Rosa.

After working at hospitals in the Bay Area, Bronzan applied to the CDC's Epidemic Intelligence Service (EIS), which provides on-the-job training in epidemiology. While waiting for her first posting, she traveled to Malawi to care for seriously ill children at Queen Elizabeth Central Hospital with Terrie Taylor, D.O., a professor of internal medicine at Michigan State University. For six months she received housing and a \$100 weekly stipend. "I thought this was a fantastic offer, although some of my friends wondered why I would be so happy about such a dramatic salary cut," she said.

In July 2000 Bronzan started her job at EIS, which over the next two



COURTESY OF RACHEL BRONZAN

Rachel Bronzan took time out from her clinical and laboratory duties for a trip to Mt. Mulanje, the largest and highest mountain in Malawi.

years took her to Mali, Kazakhstan, South Africa and Florida for work in infectious diseases.

Now, along with her malaria research, Bronzan works as a part-time clinician-researcher for Taylor. "What is unique about my position is that it allows me the opportunity to do clinical care of severely ill children, clinically related research, as well as field surveys and public health-related projects," said Bronzan.

Her epidemiological studies and program planning could affect malaria control in Africa and abroad, but she finds that caring for children afflicted with malaria is her true reward. "Although mortality is high—between 15 and 20 percent of comatose children die—those who survive tend to recover quite quickly, and the majority of them do not have long-term neurological or developmental problems. They come to the hospital in a severe coma and can walk home in as little as two or three days. That in itself is really exciting."

—Kara Nyberg

A pediatrician who treated not just the children, but the whole family

As a research fellow at Yale in 1948, **Morris A. Wessel, M.D. '43**, joined in the landmark "rooming-in" study by the late clinical professor Edith B. Jackson, M.D., which examined how keeping newborns in their mothers' hospital rooms affected families. His participation in the study also helped Wessel decide what kind of pediatrician he wanted to be.

His role in the study was to interview parents during pregnancy. Mothers- and fathers-to-be often burst into tears as they recounted traumatic childhood incidents such as the death of a parent. "Is there any way that we as pediatricians could support families during a crisis like that?" he asked himself.

Jackson and Grover F. Powers, M.D., who headed Yale's pediatric department in Wessel's student days, also led him to a broader notion of his role as a pediatrician. "Anything that affects the child's welfare is within the realm of the pediatrician's responsibility," Powers said. After graduating from the School of Medicine, Wessel worked at the Mayo Clinic under Benjamin M. Spock, M.D., MED '29, whom Wessel considered a mentor throughout his career. Wessel's training was informed by his own childhood experience. The loss of his father when he was only 11 months old and his own "various sicknesses and unhappinesses as a child" convinced him that young people needed friends and advocates whose commitment did not stop at the office door.

He found a like-minded partner in another young pediatrician, Robert G. LaCamera, M.D., FW '56, and in 1951 started a practice marked by extraordinary involvement in the lives of families and by a commitment to improve the community.

"They were always late," laughed Donna Sandillo, R.N., their longtime practice manager. They were late because they made house calls and dashed across the street to the hospi-

tal—the office was on Howard Avenue—when one of their patients was in trouble.

"People waited for them," she said. "They understood."

The doctors encouraged parents to call when they faced any major challenge—medical or not. Families appreciated touches like handwritten notes on the anniversary of a death and calls to check on teens adjusting to college. New Haven is a city of rich and poor families, and the practice saw both. They accepted homemade pies as payment for an office visit.

Wessel spread his philosophy as a clinical professor at Yale and through his writings. In 1963, he published "Why Can't Mothers Stay in Hospital With Their Children?" in *Redbook*. Mothers across the country waved the magazine in hospital admitting offices demanding, "Where's my bed? Dr. Wessel says I should stay!"

"I was not very popular," he said, ducking his head to hide a grin.

Together with Anthony Dominski, PH.D., a scientist from the School of Forestry & Environmental Studies, he investigated lead levels in children in the 1970s and recommended a level then thought to be unrealistically low. Eventually the American Academy of Pediatrics recommended an even lower level.

With former Yale School of Nursing Dean Florence S. Wald, R.N., he studied the treatment of terminally ill patients, which Wald believed was often futile and dehumanizing. Wald told Wessel his role would be to help her understand doctors' thinking. "I can't explain why doctors do what they do," he told her. But he agreed to help. Their work led to the opening of the nation's first hospice, in Connecticut, in 1974.

There he observed that friends and family were quick to comfort a surviving spouse. "Nobody paid attention to the children," he said. Wessel now writes about childhood grief and has worked in schools, dealing with everything from the loss of a beloved teacher to the loss of the class guinea pig.



Morris Wessel took a broad view of his role as a pediatrician—one marked by involvement in the lives of families.

Wessel retired in 1993, as did LaCamera three years later. Their New Haven practice moved to the suburbs, though their successors were adamant about being on a bus line so that inner-city patients would have access. Wessel works two days a week at the Clifford W. Beers Child Guidance Clinic in New Haven.

Wessel's daughter, Lois A. Wessel, R.N., M.S., a nurse practitioner working with underserved patients, said that both her father and mother, Irmgard Wessel, M.S.W., influenced her career. They "went out on a limb to help people have better lives," by addressing issues, such as housing, that are not usually the province of a physician. But her parents were not grim saints. "They clearly enjoyed what they did and were very committed to it," she said. As she accompanied them around the city, she saw patients and clients light up. "They were loved and liked and respected." Upon his retirement, hundreds of people gathered in New Haven's Edgerton Park for "Morris Wessel Day."

With HMOs mandating shorter visits and with greater technical expertise expected of physicians, Wessel worries that pediatricians are discouraged from knowing their patients as deeply as he did. "There was something about our practice that was unique," he said. "But it should not be unique at all."

—Colleen Shaddox

Tap dancing through medicine, from surgeon to song-and-dance man

While a medical student at Yale, **Brock Lynch**, M.D. '47, sang and tap danced in a hospital fund-raising play. He remembers thinking, "Should I be in show business or medicine?" But even though he'd started tap dancing when he was 8, Lynch wasn't serious about changing careers. After World War II Navy service, he resumed his medical career and decided that someday he would return to the stage.

And he has. Since he retired in 1995 from practicing general medicine at the Northampton VA Medical Center in Leeds, Mass., he has been part of Young@Heart Chorus, a Massachusetts performing troupe, in which the average age is 80. Other men and women who sing in the group were engineers, insurance executives, building contractors and teachers in their younger days. Rather than croon Cole Porter songs or others of the same vintage, the 73- to 91-year-olds sing tunes from the Rolling Stones, Bruce Springsteen, U2, the Beatles, Jimi Hendrix, Led Zeppelin and the Clash—the same loud music that they once told their children to turn down.

In the last seven years, the 22-member group has toured Europe 10 times and visited Hawaii and Australia. Lynch sings tenor and dances, although there's not much demand for tap when

you've got an electric guitar and professional drum set. Young@Heart plays to sold-out audiences in Europe; in 2001, the King and Queen of Norway gave them a standing ovation.

Because of their age, choice of music and humorous and whimsical performances, last June they were written up in *Time* magazine. The group disco dances to the Bee Gees' "Staying Alive," and Lynch is one of three soloists in "Once in a Lifetime," originally sung by the Talking Heads.

When they go abroad once a year, for a week or two, Young@Heart members face a grueling schedule, usually one performance each night over four nights. This fall, they traveled to London for two weeks, where the group performed 12 straight shows, including a matinee and evening event on a Saturday. These performances come after long plane rides and jet lag. (They always travel with three wheelchairs just in case.) The group pays tribute to each country it visits, so it may learn a song in Dutch while in Antwerp or perform Olivia Newton-John's "Let's Get Physical" in Australia.

Back in Northampton, there are weekly rehearsals, sometimes more, where Lynch and fellow members stand for two hours straight. That's a feat for anyone, but particularly for septuagenarians, octogenarians and nonagenarians whose collective conditions include arthritis, heart disease, macular degeneration, hip replacements, high blood pressure and cancer. (There are chairs at the back of the stage for anyone who gets tired.) Lynch, who jogs three times a week for 10 minutes, doesn't complain about the pace, however. "Young@Heart puts a schedule into my life," said the 81-year-old, "and without it I'd be in a rocking chair."

These days, the only rocking Lynch does is on the dance floor. But that's nothing new. Everywhere he studied or practiced medicine, he would tap dance and sing in charity hospital shows. After his New Haven theatrical debut, Lynch performed during a sur-

gical internship at the University of Cleveland Hospital and his residency at Malden Hospital in his hometown of Malden, Mass., and at New England Medical Center and St. Elizabeth's Hospital in Boston. He tapped his way through Mitchell Air Force Base on Long Island while he was chief of surgery and also when he became a teaching fellow at Memorial Sloan-Kettering Cancer Center.

Then there was more performing while in private practice with his father in Malden for 18 years, followed by more dancing and singing when Lynch moved his work life in 1975 to the Veterans Administration hospital near Northampton as a general practitioner. During the 20 years he practiced there, his surgical skills were frequently requested in the emergency room, leading to the saying, "In a Pinch, Call Lynch."

Within a month of retiring from his VA post in 1995, the self-taught tenor auditioned for Young@Heart. He danced and sang his way through "Button Up Your Overcoat" and "You're the Cream in My Coffee"—a far cry from the rock and roll he would churn out as a group member. "In show business, when you audition, the director always asks what your talent is," said Lynch. "In my case I said, 'For you, I'm a singer who dances, but if you ask me what I really am, I'm a dancer who sings.'"

He is also a doctor who dances and sings.

—Sally Abrahms

Familiar Faces

Do you have a colleague who is making a difference in medicine or public health or has followed an unusual path since leaving Yale? We'd like to hear about alumni of the School of Medicine, School of Public Health, Physician Associate Program and the medical school's doctoral, fellowship and residency programs. Drop us a line at ymm@yale.edu or write to Faces, Yale Medicine, P.O. Box 7612, New Haven, CT 06519-0612.



Brock Lynch, left, sings and dances with the Massachusetts-based Young@Heart Chorus, which specializes in classic rock.



Herold Griffith



Stephen Krant



Lloyd Friedman



Robert Hartman



Reginald Sanders



Krystn Wagner



Elizabeth Platzker and Steven Kawut

1930s

Albert W. Diddle, M.D. '36, is professor emeritus and was the original chair of obstetrics and gynecology at Memorial Research Center and Hospital at the University of Tennessee in Knoxville. The author or co-author of 131 publications on anatomy, obstetrics and gynecology and the history of medicine, he has also privately published his memoirs for his family, *U.S. Naval Duty During World War II: Key West, Florida; Guadalcanal; Okinawa; Guam; and Tientsin, China.*

1940s

B. Herold Griffith, M.D. '48, was elected an honorary member of the British Association of Plastic Surgeons. Griffith, who retired in 1996, is professor emeritus of surgery and chief emeritus of plastic surgery at Northwestern University School of Medicine.

Edward Wasserman, M.D. '45, has been named Physician of the Year 2005 by the Greater Bridgeport (Conn.) Medical Association for his volunteer work at an AmeriCares Free Clinic.

1960s

Stephen M. Krant, M.D. '69, HS '76, has been in private practice in plastic surgery in La Jolla, Calif., for 29 years, specializing in aesthetic and reconstructive surgery. He and his wife, Lyn, have established the SK Institute, a nonprofit which sponsors a monthly Breast Cancer Nite, where breast cancer survivors listen to speakers, enjoy food

and beverages and receive free spa treatments at the SK Sanctuary, which is affiliated with Krant's practice. The institute also holds melanoma, prostate and ovarian/uterine cancer nights.

1970s

Lloyd N. Friedman, M.D. '79, clinical professor of medicine at the School of Medicine, received a grant from the National Institute for Occupational Safety and Health to study new gamma interferon assays in the diagnosis of latent tuberculosis. In April he received the David Lyman Russell Award from the Connecticut chapter of the American Lung Association for contributions to the prevention and treatment of tuberculosis. Friedman is the vice president of medical affairs and the medical director of Intensive Care and Respiratory Therapy at Milford (Conn.) Hospital.

Robert H. Posteraro, M.D. '73, HS '78, FW '79, a radiologist with Lubbock Diagnostic Radiology in Texas, graduated from Oregon Health & Science University with a master of biomedical informatics degree in June.

Eddie Reed, M.D. '79, has been named the director of the Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion at the Centers for Disease Control and Prevention. He started his new position in June. Reed previously worked at the National Cancer Institute and at The Mary Babb Randolph Cancer Center at West Virginia University.

1980s

Alan B. Astrow, M.D. '80, has been appointed director of the division of hematology/oncology at Maimonides Medical Center in Brooklyn, N.Y. Astrow moved from St. Vincent's Hospital in Manhattan, where he was associate medical director of the cancer center. "We open a 50,000-square-foot state-of-the-art cancer center this fall," he writes. He is joined at Maimonides by classmate **Carl F. Schiff, M.D.** '80, who is director of rheumatology.

Robert Hartman, M.D., HS '86, writes to say that he is a clinical associate professor of dermatology at the University of Southern California School of Medicine. In October 2004 he passed a new board exam in pediatric dermatology. For four months each year he heads a pediatric dermatology clinic at Childrens Hospital in Los Angeles.

Reginald J. Sanders, M.D. '85, HS '86, chief of the retinal service at the Georgetown University/Washington National Eye Center, was named one of the top physicians in the Washington, D.C., metro area by *Washingtonian* magazine in July. Sanders also serves on the board of the American Society of Retina Specialists.

Krystn R. Wagner, PH.D. '89, M.D. '96, assistant professor of medicine (infectious diseases/AIDS program) at the School of Medicine, and José F. Salvana, M.D., an infectious disease specialist, were married in May in Baltimore. Wagner is the medical director of the Nathan Smith HIV clinic at Yale-New Haven Hospital. Salvana is the HIV clinical director at the Hill Health Center, a community clinic in New Haven.

1990s

Alison L. Days, M.D. '99, and Sergio Rico Jr., M.B.A., were married in Cancún, Mexico, in February. Days is a pediatrician at Texas Tech University in El Paso, and her husband is a maintenance supervisor at Penske Truck Leasing.

Mauricio J. Garrido, M.D. '98, a cardiothoracic surgery fellow at Columbia University Medical Center in New York, and Louisa Terry, an executive director of the Ovarian Cancer Research Fund, a nonprofit agency in New York, were married on April 9 in Miami.

Steven M. Kawut, M.D. '95, the Herbert Irving Assistant Professor of Clinical Medicine in Epidemiology at the Columbia University College of Physicians and Surgeons, and Elizabeth S. Platzker, a senior designer at Liz Claiborne, the clothing and accessories company, were married on May 29 in Los Angeles. Kawut teaches and conducts research on pulmonary hypertension and lung transplantation.



Zimra Gordon

James Moore

Andrea Pernack, M.P.H. '98, a program officer at the Institute of Medicine, and Dean Anason were married on May 1, 2004, in Warren, Mich. Pernack, now Pernack-Anason, has worked on studies involving the national smallpox vaccination program and data sharing for a vaccine safety research database.

Lynn E. Sullivan, M.D. '96, HS '00, was married to David A. Fiellin, M.D., HS '95, FW '97, in September in South Salem, N.Y. Sullivan is an assistant professor of medicine at the School of Medicine, where Fiellin is an associate professor of medicine.

2000s

Cristina Baseggio, M.D. '05, was married in May to Seth Alexander, a director of investments in the office of the Yale Endowment. Baseggio began a residency in internal medicine at Brigham and Women's Hospital in Boston in June.

Jonathan Solomon Erulkar, M.D. '01, and **Deirdre "Dede" Holden Carroll**, M.S.N. '00, A.P.R.N., were married on August 1, 2004, in Lake Forest, Ill. Fellow Yale Medicine grads who attended included John Abraham, M.D. '00, and Badri Rengarajan, M.D. '99. Erulkar is in his fifth year and a chief resident in the Department of Orthopaedic Surgery and Rehabilitation at

Yale. Carroll, a psychiatric clinical nurse specialist and adult nurse practitioner, is a third-year PH.D. student at Boston College. Previously she spent several years as a co-investigator in the Clinical Trials Program at the Yale Child Study Center and on the clinical faculty of the Yale School of Nursing. Since their honeymoon on Anguilla, the newlyweds have settled into married life in Branford, Conn. In 2006, however, they will be moving to Boston, where Jonathan has accepted a spine surgery fellowship at the New England Baptist Hospital and a clinical faculty appointment with Tufts University School of Medicine.

Zimra J. Gordon, M.P.H. '02, D.V.M., and Steven J. Danzer, PH.D., were married on April 17. Gordon is a veterinarian at the Rippowam Animal Hospital in Stamford, Conn., and a research associate with the Yale Occupational and Environmental Medicine Program. Danzer is an environmental planner for the town of Stratford, Conn.

Elizabeth W. Holt, M.P.H. '05, and Matthew J. Delfino Jr., M.B.A., were married in June in Greenville, S.C. After their honeymoon, the couple moved to Boston, where Delfino is employed at Brigham and Women's Hospital.

Anita Karne, M.D. '02, and Mehul A. Dalal, M.D., M.Sc., were married in July in Knoxville, Tenn. Karne is chief resident in primary care at New York University School of Medicine. Dalal is an attending physician in medicine at N.Y.U.-Bellevue Medical Center.

Matthew P. Kronman, M.D. '03, was married in September to Evelyn K. Hsu, M.D., in Seattle. They met at Children's Hospital in Seattle, where both were residents in pediatrics.

D. Scott McBride Jr., M.D., HS '05, completed a residency in anesthesiology in June and is now a staff anesthesiologist with the U.S. Air Force at Elmendorf Air Force Base near Anchorage, Alaska. He's scheduled to be deployed to Iraq in May 2006 to serve in a field hospital.

James Moore, M.P.H. '03, is one of 10 fellows selected to participate in the newly established Association of Schools of Public Health/Centers for Disease Control and Prevention (CDC) International Global AIDS Fellowship Program. The program is part of CDC's Global AIDS Program, which is part of President Bush's five-year initiative to channel \$15 billion into HIV/AIDS treatment and prevention in 12 African countries and Guyana and Haiti.

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William T. Bachmann, M.D., HS '74, died on July 28 of cancer. He was 65. Bachmann, a dermatologist, lived in Stonington, Conn., and maintained a practice in Westerly, R.I., for more than 30 years. During the Vietnam War Bachmann served as a physician on submarines based in Groton, Conn. He was known in the area not only as a physician, but also for his enthusiasm for fishing for tuna and marlin. In recent years he began exploring area wildlife by boat and kayak. An activist and defender of healthy sea life, he recently completed a book about his fishing experiences and environmental insights.

Horst N. Bertram, M.D., HS '59, a radiologist, died on March 12 in Cornwall, Pa. A native of Berlin, Germany, Bertram completed his medical studies at the end of World War II, then began a residency in Ohio. After serving as a battalion surgeon in the Army during the Korean War, he came to Yale to complete his residency in radiology. In 1965 he joined the staff of the Good Samaritan Hospital in Lebanon, Pa., where he stayed for 30 years. He served as chair of the radiology department and president of the Lebanon County Medical Society.

Sister Mary Anne Fitzmaurice, R.N., M.P.H. '69, a member of the Sisters of St. Joseph, died on May 1 in West Hartford, Conn. She was 80. Fitzmaurice received her nursing degree from St. Francis Hospital School of Nursing in Hartford, Conn., and in 1955 became operating room supervisor at St. Mary's Hospital in Waterbury, Conn. In 1967 she began studies in hospital administration at Yale. After her graduation in 1969 she spent a year at the Hospital of St. Raphael in New Haven as a resident in administration. During her career she also worked at St. Francis Hospital in Hartford, the Provincial House of the Sisters of St. Joseph in West Hartford and the Intensive Education Academy in West Hartford. She was honored with a Certificate of Membership in the American College of Hospital Administrators, and in 1979 the mayor of Hartford recognized her service with a Certificate of Award.

Frederick P. Glike, M.D. '41, died on September 12 at his home in Meriden, Conn. He was 89. A lifelong resident of Meriden, Glike graduated from Harvard University before entering the medical school at Yale. During World War II he was a captain with the Third Battalion and participated in the Battle of the Bulge. He returned to Meriden, where he practiced medicine for 40 years until his retirement. Glike loved music and played the clarinet in the Meriden

Symphony. He also enjoyed the outdoors and took hiking trips with his family in the White Mountains, where he climbed all peaks over 4,000 feet.

Victor C. Hackney, M.D. '43, died on September 5 in Geary, Okla. He was 88. During World War II Hackney served in the Navy. Board certified in dermatology and pathology, he studied at the Armed Forces Institute of Pathology. He received academic appointments at the University of Southern California and at Stanford University before becoming founding chair of dermatology and professor of dermatology and pathology at Indiana State University School of Medicine. He retired in 1976.

H. David Kearing, M.D., HS '68, died on September 9 at his home in Brackney, Pa. He was 68. After receiving his medical degree from Cornell in New York, Kearing completed a residency in ob/gyn at Yale. He subsequently served in the U.S. Army at West Point for two years. From 1972 to 1991 he practiced ob/gyn in Binghamton, N.Y., with two partners, then went into private practice until 2001, when he retired.

Carter Lee Marshall, M.D. '62, M.P.H. '64, died on February 18 in Tucson, Ariz. After service in the Army, Marshall was on the faculty at the University of Kansas School of Medicine, the Mt. Sinai School of Medicine and the City University of New York. In the 1970s he helped set up a medical school at Morehouse College in Atlanta. He later served as director of medical education at the University of Medicine and Dentistry of New Jersey, before moving to Arizona to work at the Health Services Advisory Group, the state's Medicare quality improvement organization. He co-authored an introductory text for allied health workers and published more than 70 articles.

Willys M. Monroe, M.D. '41, a pathologist, died on March 18 in Lynchburg, Va. Monroe was a life fellow of the College of American Pathologists, a fellow of the American Society for Clinical Pathology and a life member of the Medical Society of Virginia. During his career he spent five years in the U.S. Public Health Service, leaving as a lieutenant colonel to become chair of the department of pathology at Richmond Memorial Hospital, where he established a blood bank and trained lab technicians. He also taught pathology at Virginia Commonwealth University and the University of Virginia. He was the first chief of the Richmond Metropolitan Blood Service.

Richard B. Ogrean, M.S. '52, died on June 2 in Fort Myers, Fla. He was 83. After serving in the U.S. Army Medical Corps in Europe during World War II, Ogrean obtained a degree in public health administration at Yale, then worked as an assistant administrator at Yale-New Haven Hospital. In 1956 he became an administrator at Windham Community Memorial Hospital in Willimantic, Conn., where he stayed for 18 years. He worked at other hospitals until his retirement in 1983. He was also a deacon at the First Baptist Church in Willimantic.

Howard Rasmussen, M.D., PH.D., a former professor of medicine and cell biology and chief of endocrinology and metabolism at the School of Medicine, died on April 20 in North Carolina after a long illness. He was 80. Rasmussen was one of the first scientists to recognize the importance of calcium as a signaling molecule. During his career he was chair of biochemistry at the University of Pennsylvania and founding director of the Institute of Molecular Medicine and Genetics at the Medical College of Georgia. Rasmussen was at Yale from 1976 to 1993.

Robert T. Sceery, M.D. '50, died on February 18 of congestive heart failure in Cohasset, Mass. He was 84. Sceery, a pediatrician, was school physician in Cohasset for more than 40 years. Known for his quiet manner, he made house calls and saw patients regardless of their ability to pay. Although retired for several years, Sceery saw occasional patients and attended weekly rounds at Massachusetts General Hospital. During World War II he joined the Navy, piloting a tank landing ship to Normandy beach on D-Day and participating in assaults on southern France and Japan.

Paul W. Sternlof, M.P.H. '57, died in Sharon, Conn., on August 12. He was 73. Sternlof served as assistant administrator of Baltimore General Hospital in Maryland from 1958 until 1962, when he became president of Sharon Hospital. He remained in that post until 1989.

Daniel B. Stryer, M.D. '90, director of the Center for Quality Improvement and Patient Safety at the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services, died on May 19 in Rockville, Md., of complications from a brain tumor. The center provides information to patients and the health care industry to improve quality of care. Stryer took on his job in 1997, after a residency in internal medicine at the University of California, San Francisco, and,

with his wife, pediatrician Stacy Beller Stryer, M.D. '91, spent three years with the Indian Health Service in Arizona.

George Tyler, M.D. '67, died on August 28 in Bethlehem, Pa. He was 65. Tyler, a fellow of the American College of Surgeons, was a senior surgeon at Lehigh Valley Hospital-Muhlenberg and an instructor for the "Advanced Trauma Life Support" course. He was a major in the U.S. Army Seventh Cavalry and served in Vietnam, where he received the Bronze Star.

Vernon T. "Doc" Watley, M.D. '49, died on August 30 in Beaumont, Texas. He was 83. In March 1942 Watley enlisted in the U.S. Air Force and served at what later became Lackland Air Force Base in Texas. During the Korean War he was called back to duty and ran the neurological service at Lackland. After his military service, he was the superintendent of Abilene State Hospital for Epileptics and a psychiatrist at Austin State Hospital. During his career he was also an emergency room doctor and, until his retirement in 1981, a family physician.

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MICHAEL MARSLAND

A "perfume" to prevent disease

Early in 1999 John R. Carlson, PH.D., the Eugene Higgins Professor of Molecular, Cellular and Developmental Biology, reported that his laboratory had identified 16 odor receptor genes in fruit flies (See "Researchers Discover Odor Receptor Genes in Fruit Flies," Spring 1999). It was the first finding of such genes in insects. Carlson and his colleagues went on to find taste receptor genes in fruit flies and to identify the functions of specific odor receptors in mosquito antennae.

Now Carlson's laboratory is part of an international team that plans to harness those findings to reduce the spread of malaria, which kills 1 million people each year, mostly in the developing world. The female mosquitoes that spread the disease are drawn to certain human odors, which they "smell" with receptors in their antennae. The team, which includes scientists in the United States, the Netherlands, Tanzania and Gambia, hopes to create a "perfume" that will either lure malaria-carrying mosquitoes into traps or act as a repellent.

Scientists at Yale and Vanderbilt University will identify odors that affect mosquitoes and will create the "perfumes." Dutch researchers will study the effects of the odors on mosquito behavior in the laboratory. And the African scientists will field-test the odors. The \$8.5 million, five-year project is funded by the Bill & Melinda Gates Foundation's Grand Challenges in Global Health initiative. Ultimately, the scientists hope the odors they develop will prevent malarial mosquitoes from infecting humans, and will be inexpensive, safe and easy to use in rural areas. This approach could also be applied to mosquitoes that carry dengue fever or the West Nile virus. "With insect-borne diseases, the best way to control the disease is usually to control the insect," Carlson said. "We smell good to the mosquitoes, so if we can understand in molecular detail how the insects are attracted to us, we might be able to devise new means of controlling them."

—John Curtis



JANUARY 1955

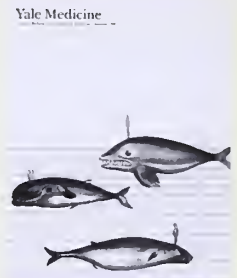
Alumni Bulletin

Students' Loan Fund of Yale Men in Medicine

"The following statement is published at the request of the officers and incorporators of the Students' Loan Fund of Yale Men in Medicine, Inc.

"It is estimated that it costs a student a minimum of \$2,000 for each of his four years of residence at the Yale University School of Medicine. Although this represents only a fraction of the total cost of his medical education, it is nevertheless a considerable sum. ... In the present academic year, ninety students, or twenty-seven percent of the student body, have requested such help. ...

"The Students' Loan Fund of Yale Men in Medicine has been for twenty years a modest but continuing source of help to our needy and worthy students. Since its inception in 1934, this Fund has provided loans to one hundred and twenty of our students."



SUMMER 1980

Yale Medicine

Human Genetics finds a new home

"The completion of the third floor of the Nathan Smith Building has long been awaited by members of the Department of Human Genetics. 'It seems as though we had outgrown facilities in the LCI building even before we moved in,' a faculty member observed recently.

"During the past two decades, the study of human genetics has become one of the most rapidly advancing and challenging fields in medical science. 'It is hard to believe now, that in the 1950s when I and many of my colleagues were in medical school, human genetics was a relatively minor subject,' Dr. Leon Rosenberg, chairman of the Department, remarked a few years ago.

"The Nathan Smith Building ... symbolizes the spirit in which the Department was founded in 1972. At the time, Dr. Rosenberg stated, 'The fundamental philosophy behind this departmental organization is that the application of basic genetic knowledge to the problems of human illness can best be accomplished in a climate which encourages close interaction between those with expertise in basic laboratory genetic science and those who are concerned with patients with genetic problems. This is a new concept in academic medicine.'"

in an envelope with a photograph to

Claire M. Bessinger, Yale Medicine Publications,
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TULANE STUDENTS FIND A SAFE HAVEN AT YALE

Dorota Ruszczyk had just returned to New Orleans from fieldwork in Kenya when she learned that Hurricane Katrina was about to land. She and her fiancé stocked up on food, batteries and water, but as the storm approached, they left for Baton Rouge. Now Ruszczyk is with her family in New Haven and finishing her M.P.H. course work at Yale rather than Tulane. Memories of the days after the storm still haunt her. "You saw everyone around you with a blank stare on their face," she said. The hurricane diverted Andrea Humphrey, M.P.H. '05, from a doctoral program at Tulane back to Yale, where her former advisors helped her sign up for course work. Although her clothes, computer and textbooks are in New Orleans, Humphrey considers herself lucky. "It's going to be very hard for people to get their lives back together," she said. David Grew, who was about to enter public health school at Tulane, is taking classes at Yale. He weathered the storm with his landlord's family in Houma, La., then spent time in Texas, including a day helping evacuees in Austin. "It had a real effect on me, in how I look at the way health care should be distributed," said Grew.

Grew, Humphrey and Ruszczyk are among five students from Tulane who have found temporary homes at the medical school after Hurricane Katrina forced the closing of Tulane University in late August. While the public health students are in the classroom, two Tulane medical students are at Yale for clinical clerkships.

The day before Hurricane Katrina struck, fourth-year Conar Fitton left New Orleans with "three T-shirts, a pair of flip-flops and a dog." Stephanie Malliaris, a third-year, had left a day earlier. "Most people leave for hurricanes thinking they'll be back home in three or four days," she said. Fitton spent two weeks at Yale in a hepatology rotation. Malliaris stayed eight weeks for a pediatrics clerkship. In September Tulane relocated its medical school to Houston. Other Tulane programs are expected to resume in January in New Orleans.

—John Curtis



Andrea Humphrey, center, who received her M.P.H. from Yale in May, returned to New Haven in September after Hurricane Katrina led to the closing of Tulane University, where she was about to begin doctoral studies. At Yale she took classes and also found work as a teaching assistant.

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Yale Medicine

spring 2006

Six Yale faculty
named to IOM

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Yale connections
around the world

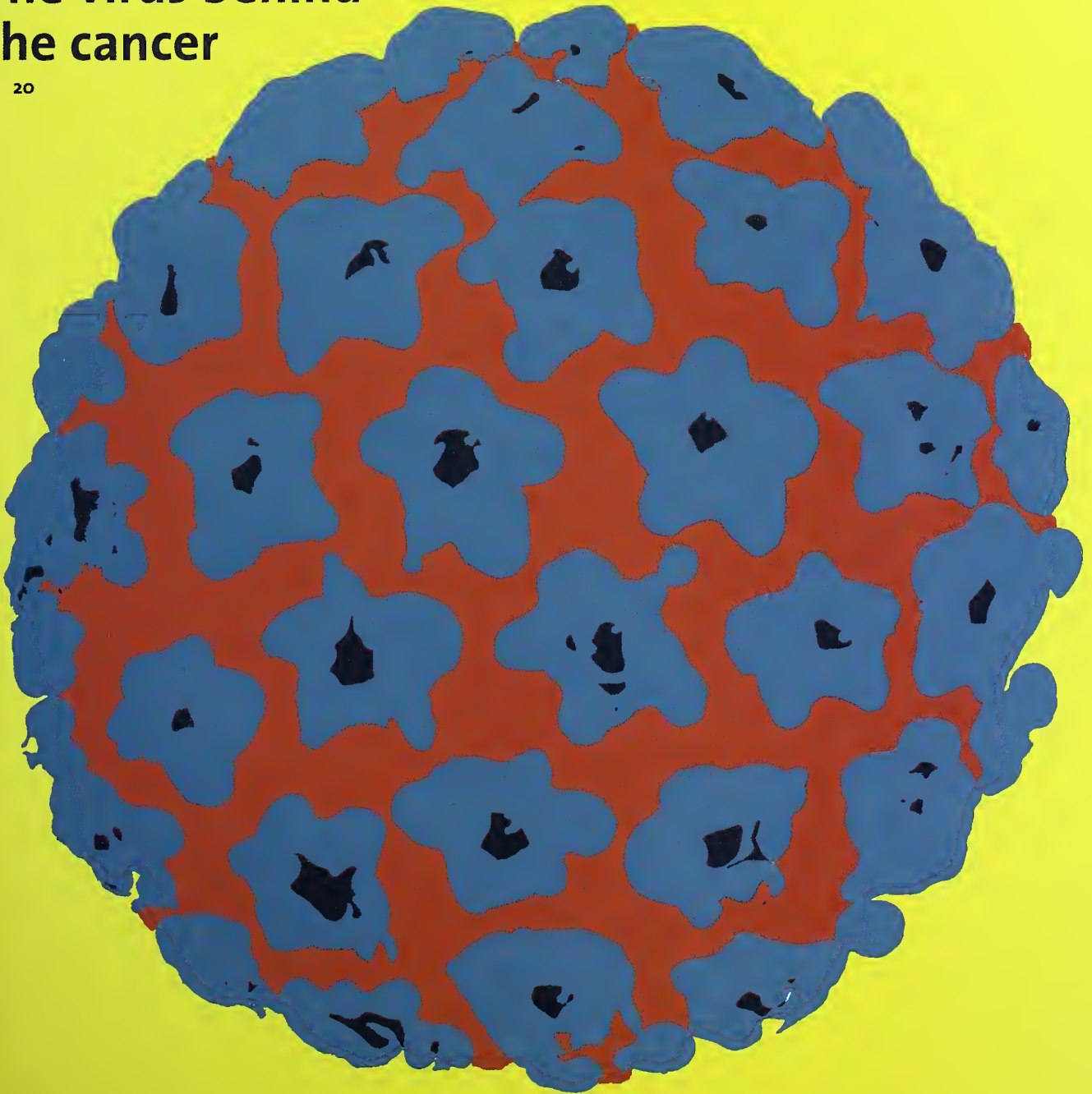
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SPRING 2006

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A medical student's summer research journey becomes a Yale (and family) reunion like no other.

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Over the last half-century research has produced strong evidence of viral links to some cancers. Now vaccines may protect against both.

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ON THE COVER

The human papillomavirus (HPV) is a common infection spread through sex and skin-to-skin contact. Since 1975 it has been linked to cervical cancer.

BACKGROUND

HPV has helped scientists understand how a virus can lead to cancer. It is a member of a family of small DNA viruses that typically cause benign warts. But some high-risk HPV types have been linked to carcinomas, including cervical cancer. The virus is also thought to play a role in other anogenital cancers, skin cancers and some head and neck tumors.

Illustrations by Yasuo Tanaka



HOW TO REACH US

Yale Medicine welcomes news and commentary. Please send letters to the editor (350 words or less) and news items to *Yale Medicine*, P.O. Box 7612, New Haven, CT 06519-0612, or via electronic mail to ymm@yale.edu, and include a daytime telephone number. Submissions may be edited for length, style and content.

VISIT US ON THE WEB

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News of my demise is premature

According to the alumni reunion report for the Class of 1960 published in the Autumn 2005 issue of *Yale Medicine*, Jerrold M. Post, M.D. '60, led the class in "a brief silence in honor of our deceased classmates," including me. While I am deeply honored, I am completely undeserving.

My wife, Rosemary, died three years ago. I am running an active research program at the University of Connecticut Health Center. I have participated in the Class of 1959 reunions, since I was closer to them, having taken a year off after the third year to do research before graduating.

*D. Kent Morest, M.D. '60
West Simsbury, Conn.*

Dishonest reporting in Vietnam and PTSD

As a combat surgeon in DaNang in 1968, I experienced the Tet Offensive firsthand and saw more carnage than most civilian surgeons see in a lifetime. Cathy Shufro's "The Unseen Wounds of War" [Autumn 2005] brings back memories—and prompts a few questions.

Dishonest media coverage of Vietnam, specifically the reporting of the Tet Offensive as a defeat of our forces, was the reason our veterans returned to a hostile public.

Did any of Ms. Shufro's vets mention that our forces never lost a significant battle in Vietnam? Did Ms. Shufro run across data showing that victorious combatants who return to be hailed as heroes suffer less post-traumatic stress disorder than do defeated forces? Could the confusion of returning to be spat upon and subjected to the disrespect and dishonor ordinarily reserved for the vanquished—*after defeating the enemy decisively in every encounter*—be a factor in the symptoms experienced by those in Ms. Shufro's group?

*Martin L Fackler, M.D. '59
Retired Col.,
U.S. Army Medical Corps
Gainesville, Fla.*

Chase leaving to study what makes good doctors

In December the medical school's deputy dean for education, Herbert S. Chase Jr., M.D., announced that he would be ending his six-year tenure at the end of the academic year on June 30. Chase will return to Columbia University's College of Physicians and Surgeons, where he spent 22 years before coming to Yale, to continue his research into the kind of teaching that makes a good doctor. "I am interested in looking at physician performance and patient outcomes, and asking whether and how one's medical educational background influences the quality of a physician's performance," Chase said.

Recruited in 1999, Chase was asked to evaluate the medical school curriculum and recommend and implement changes necessary to meet the challenges of a new landscape in medicine. He championed the merging of courses in related disciplines and encouraged a more fluid curriculum that would integrate the basic and clinical sciences over four years of study. As deputy dean he oversaw the revamping of the anatomy course for first-year students; the creation of the Society of Distinguished Teachers to reward outstanding faculty; and the implementation of the Clinical Skills Program, which provides rigorous instruction and assessment during the first two years of medical school. According to Dean Robert J. Alpern, M.D., "Yale has benefited greatly from [Chase's] commitment, enthusiasm and dedication to the medical students, and we take great pride in Herb's accomplishments as deputy dean."

Chase said that credit for his achievements is not his alone. "Whatever was accomplished, was accomplished with great effort by dozens of faculty."

—John Curtis

Yale medicine

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A world of connections

This issue's feature lineup begins with a tale of connections—among Yale alumni and faculty, among doctors and patients and among old school friends. As related by Jill Max, these connections made it possible for a Yale medical student to do research in Italy, and also for her mother in Serbia to receive a critical, life-changing procedure.

For our cover story, "The Virus Behind the Cancer," Contributing Editor Jennifer Kaylin looks at a different type of connection. She traces the guesses, speculation and discoveries that led scientists to the viruses that underpin about 10 percent of all cancers. Those connections between viruses and cancer could yield clues that will put scientists on the path to vaccines and treatments.

Contributing Editor Marc Wortman donned a jumpsuit and entered the pathology labs to observe an autopsy for his article, "The Final Chapter." Wortman examines why autopsies are so rarely done, even though it is through the autopsy that all of the patient's medical history is connected in the last, most complete picture of his or her health.

Finally, in "When Animals Sound a Warning," Rhea Hirshman explores the connections between human disease and the environment. Her research took her back to Captain Cook's discovery of Hawaii and the first Italian invasion of Ethiopia. In both instances new creatures introduced new

diseases, forever altering the ecology and epidemiology of those lands. That interaction is the focus of Yale's new Center for EcoEpidemiology, which brings together scientists in both fields.

In the spring of 2004 we asked Amelia Shaw, M.P.H. '03, who was in Haiti on a Fulbright Scholarship and making a documentary film about AIDS, to write about her experiences. Shaw cautioned us that although she'd interned at National Public Radio, she'd never written a feature-length magazine article. Her first drafts convinced us we'd made the right choice. Shaw's passion and commitment infused every page of her story ["A Film to Finish," Fall/Winter 2004].

This spring the Association of American Medical College's Group on Institutional Advancement seconded our opinion by honoring Shaw with a Robert G. Fenley Writing Award of Excellence for her article. The award, given annually, recognizes outstanding writing. We couldn't agree more. Congratulations, Amelia.

John Curtis
Managing Editor
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SECOND OPINION BY SIDNEY HARRIS



"APPARENTLY, MR. FIADKIN, EVOLUTION IS
A TWO-WAY STREET."



TERRY DAGRA DI

The Institute of Medicine elected a record number of Yale scientists to its ranks last year. From left, Pietro De Camilli, Gerald Shulman, Joan Steitz, Kelly Brownell, Margaret Grey and Joseph Schlessinger, joined by Carolyn Slayman and Dean Robert Alpern.

Six at Yale named to Institute of Medicine

Top honor goes to experts in drug development, diabetes, obesity, neuroscience and genetics.

Six Yale researchers, five from the School of Medicine and one from the School of Nursing, were elected to the Institute of Medicine (IOM) of the National Academies in October. Their election brings the number of Yale scholars in the IOM to 37, including two at the School of Management and one at Yale-New Haven Hospital.

"It is unprecedented in recent memory that so many from our institution have been elected in a single year," said Dean Robert J. Alpern, M.D., Ensign Professor of Medicine. Previously, according to IOM records, no more than three Yale scientists had been elected in one year. These elections, Alpern said, give Yale one of the highest concentrations of members of any institution in the nation.

The six were honored at a reception in the Medical Historical Library in December.

Elected this year are Kelly D. Brownell, PH.D., chair and professor of psychology, professor of epidemiology and director of the Rudd Center for Food Policy & Obesity; Pietro De Camilli, M.D., FW '79, the Eugene Higgins Professor of Cell Biology and a Howard Hughes Medical Institute investigator; Margaret Grey, R.N., DR.PH., the Annie Goodrich Professor of Nursing and dean of the School of Nursing; Joseph Schlessinger, PH.D., the William H. Prusoff Professor of Pharmacology and chair of pharmacol-

ogy; Gerald I. Shulman, M.D., PH.D., professor of medicine and of cellular and molecular physiology and a Howard Hughes Medical Institute investigator; and Joan A. Steitz, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry.

Brownell is perhaps best known for his efforts to curb obesity, which form part of his studies of the intersections of behavior, environment and health. De Camilli is a cell biologist interested in understanding molecular mechanisms in presynaptic function and the role of phosphoinositide metabolism in the regulation of membrane traffic. Schlessinger's lab studies the mode of action of growth factor receptors and the intracellular signaling pathways that are activated by growth factor stimulation. Shulman is an expert on the mechanisms of insulin resistance, the role of the liver and muscle in the pathogenesis of type 2 diabetes and the benefits of exercise in diabetes management. Steitz discovered snRNPs, small particles in cells that are necessary to convert genetic information into active proteins. Grey is renowned for her studies of adaptation to chronic illness in childhood, particularly in children with type 1 diabetes mellitus.

The Yale researchers are among 64 new members elected to the IOM in 2005. The IOM was established in 1970 by the National Academy of Sciences to honor professional achievement in the health sciences and to serve as a national resource for independent analysis and recommendations on issues related to medicine, biomedical sciences and health.

—John Curtis

A son of Yale and the medical school receives AYA's highest honor

At the end of World War II, Nicholas P.R. Spinelli, M.D. '44, took leave from his Army unit in Germany and hitched a ride on a cargo plane to Rome. From there he traveled to Faeto, a village in southern Italy overlooking the Adriatic Sea that his parents had left 30 years earlier, where the villagers celebrated the arrival of their native son. "I was there for three nights," Spinelli said. "I had to make rounds and visit every sick person in the village."

His triumphant return to his family's ancestral community was the result of his parents' belief in education and Spinelli's own belief in the value of his education at Yale, where he earned his undergraduate and medical degrees. Had they stayed in Italy, Spinelli said, his parents would never have been able to educate their yet-unborn children, Nicholas and his sister, Viola, M.P.H. '65. "Education was a passion with both my parents. That was why they were working so hard," he said.

Throughout his career Spinelli has shown his loyalty to Yale by raising money for the school, establishing with his classmates a scholarship fund, serving as the medical school's director of alumni affairs and sponsoring the first White Coat ceremony in 1992.

In November the Association of Yale Alumni awarded Spinelli the Yale Medal, which, since 1952, has honored outstanding service to the university. In this recognition, Spinelli joins such other medical school graduates and faculty as pediatrician Grover F. Powers, M.D.; Russell B. Scobie, M.D. '29; William L. Kissick, M.D. '57, M.P.H. '59, DR.PH. '61; Muriel D. Wolf, M.D. '59, HS '60; and the legendary Dean Milton C. Winternitz, M.D.

Spinelli's path to Yale began in Stratford, Conn., where his parents had settled. His father ran a succession of businesses, including a gas station

and restaurant on the Boston Post Road, the main thoroughfare between New York and Boston.

In 1937 Spinelli entered Yale College, planning to become a writer. At the end of his freshman year, however, he took a job in a biology laboratory, where a professor encouraged him to study medicine, and in the fall of 1941 he entered the School of Medicine.

A few months later, while preparing for an anatomy exam, he heard President Roosevelt announce on the radio that the nation was at war. Spinelli and his 42 classmates were inducted into the Army, and their medical education was accelerated to meet wartime needs. Upon his discharge Spinelli returned to Stratford to practice internal medicine. A heart attack forced his retirement in 1958, but he began a second career as director of medical education at Bridgeport Hospital. In the 1980s his second career gave way to a third career as director of alumni affairs at the medical school. His main concern there was what he called "incubating alumni," strengthening relations with students and bringing them into the fold by including them in alumni events. At that time he helped create the Committee on the Well-Being of Students, which makes a report each year on issues of concern to students.

Perhaps his greatest gift to the medical school was his proposal to his classmates at their 40th reunion in 1984. He asked them to contribute to a scholarship fund over the next decade. By then, he said, the fund would be large enough to offer its first scholarship. In 1994, with 100 percent participation from the class, the fund paid half the expenses of a first-year student. Eleven years later the fund was supporting up to three students through their first year.

"I have gotten letters from students who have been given the scholarship, saying how important it was and how they couldn't have gone to medical school without it," Spinelli said.



For his long-standing service to the university and the School of Medicine, Nicholas Spinelli received the Yale Medal from the Association of Yale Alumni. At the ceremony in November Spinelli signed the President's Book.

For his service to Yale, Spinelli received the Distinguished Alumni Service Award from the Association of Yale Alumni in Medicine in 1987 and the Peter Parker Medal in 1994. In recognition of his contributions to the medical school, two rooms were named in Spinelli's honor in 2000, the medical school's Office of Alumni Affairs and one at the Center for Neuroscience and Regeneration Research at the VA Connecticut Healthcare System in West Haven.

But no honor, he said, surpasses the first he received from the university when he was 16 years old. "The greatest gift I got was the letter saying I was accepted to Yale."

—J.C.

From Student Research Day to a scholarly publication and *The Wall Street Journal*

Last May at Student Research Day, Hardean Achneck, M.D. '05, described a link between atherosclerosis and aortic aneurysms. The aneurysms, he found, seemed to protect against atherosclerosis, a deadly form of arteriosclerosis.

By summer's end Achneck's research was published in the journal *Chest* and reported in *The Wall Street Journal*. Achneck was first author of the journal paper; the senior author was his advisor, John A. Elefteriades, M.D. '76, HS '81, FW '83, professor and chief of cardiothoracic surgery. "I am very happy to see the results become so well-received," said Achneck, now

a surgical resident at Duke University School of Medicine.

The research began years ago and arose from repeated observations in the operating room. "Operating every day we noticed that in patients with aneurysms at the top of the chest, their arteries were pristine," said Elefteriades. "They were like babies' arteries, teenagers' arteries." Typically, he said, even men in their early 20s have fatty streaks and plaque in their arteries.

Elefteriades has long welcomed medical students working on their theses, and he first assigned this project to Biren P. Modi, M.D. '02. With the research still ongoing when Modi graduated, Achneck picked up the project and spent a fifth year at Yale working on it.

Literature searches, he said, yielded no articles exploring the links between two types of aneurysms located in the ascending aorta—annuloaortic ectasia and type A dissection—and atherosclerosis. The next step was to find 64 patients with both types of aneurysm, and a control group of 84 patients with no history of aneurysms. The control patients came from the emergency department, where they had received treatment for trauma and had had CT scans of their chests.

The patients who had aneurysms, the study found, were less likely to have atherosclerosis. This was independent of all common risk factors for atherosclerosis. "It was a statistically powerful finding," Elefteriades said, adding that it fits with the results of laboratory research. "There are some strains of rodents that have been developed that are prone to aneurysms, and they are protected from arteriosclerosis."

Why and how aneurysms offer protection from atherosclerosis remains unclear. Elefteriades and his colleagues are looking at enzymes called matrix metalloproteases (MMPs), which degrade material that accumulates on arterial walls. "It may be, and this is not proven," said Achneck, "that some of these MMPs are causing aneurysms on the one hand and chewing up atherosclerosis on the other.

The gene for MMP3 is on a section of chromosome 11 that is known to cause mutations that increase the risk of aortic aneurysms. Elefteriades and colleagues are working with Celera Diagnostics to explore the underlying genetics.

Since his graduation Achneck has been focusing on his residency. "I'm trying to survive," he said.

—John Curtis



Yale researchers believe that aortic aneurysms, such as the annuloaortic ectasia aneurysm shown above, protect against atherosclerosis.

KESSLER PORTRAIT UNVEILED

David A. Kessler, M.D., former dean of the medical school, returned to the Sterling Hall of Medicine in December for the unveiling of his official portrait by artist Richard Whitney. At a ceremony in the Historical Library, colleagues and Yale President Richard C. Levin lauded the achievements of Kessler's tenure from 1997 to 2003, specifically the construction of the Anlyan Center for Medical Research and Education and the recruitment of 11 department chairs. Kessler said that although the portrait is of one person, many people contributed to his accomplishments as dean. "These things do not happen alone," he said.





New five-year public health program gives undergrads a head start

Yale junior Sarah Milby has always been interested in pursuing a career in public health and community development, and a new joint-degree program may be able to give her a head start. Milby, a premed and history of science/medicine major, plans on being one of the first applicants to a new five-year joint-degree program that will allow her to earn a B.A. or B.S. at Yale College and an M.P.H. from the Yale School of Public Health (EPH). "I'm so excited to start preparing for my career in public health as a senior," she said.

The program is designed to give students a broad understanding of the factors that shape public health and to equip them with the tools necessary to address public health issues, such as the fight against chronic disease and the impact of environmental stressors on human health. It is open to all undergraduates, regardless of their major. Students would normally apply to EPH during the spring of their sophomore year, but juniors may also apply this spring, when the first wave of applications will be considered.

Developed over the past two years, the program is a response to increasing student interest in the field of public health and serves as an alternative to the two-year master's program already in place. "There has been evident a very large demand on the part of undergraduates, who are agitating for more course experiences and educational opportunities that allow them to take their classroom knowledge and put it into more concrete and applied

settings," said Mark J. Schlesinger, PH.D., director of undergraduate studies at EPH and professor in the Division of Health Policy and Administration. He also views the program as an opportunity for EPH to connect itself more extensively with Yale College.

In addition to completing the requirements for their undergraduate major, students in the new program will complete six public health courses, such as health policy, biostatistics and principles of epidemiology, during their junior and senior years. Between the fourth and fifth year they will complete a public health internship, and during the fifth year they will be enrolled full-time at EPH in one of the school's eight divisions, where they will complete 10 courses and a master's thesis.

The five-year program and a new one-year mid-career program for health care professionals will bring both older and younger students to EPH. "Each group will bring its own distinctive resources into the classroom," said Schlesinger. "I think it will make the classroom experience much richer for all the students."

For undergrads who are anxious to begin earning a graduate degree in public health while working toward their bachelor's degree, the combined program is a welcome addition. "I want to start my life and make a difference," said Milby. "That's why this is just too good to be true."

—Jill Max

et cetera...

GERMAN PHARMA FUNDS RESEARCH

The School of Medicine and Boehringer Ingelheim Pharmaceuticals Inc. (BIPI), the Ridgefield, Conn.-based division of the German pharmaceutical firm, have formed an alliance to explore treatments for cardiovascular, inflammatory and autoimmune diseases. Under the agreement, formalized last July, BIPI will fund research projects at Yale, several of which are already under way. The projects are investigating the role of inflammation in organ rejection and atherosclerosis; channels that admit calcium into immune system cells; enzymes that act in the kidneys to regulate salt and fluid balance; and the formation of new blood vessels in the heart.

"Yale, with its excellence in immunology and cardiovascular research, offers a real opportunity for mutual benefit," said Mikael Dolsten, M.D., PH.D., head of corporate division pharma research at BIPI's world headquarters in Ingelheim, Germany.

BIPI will work with scientists in the Section of Immunobiology and in the Interdepartmental Program in Vascular Biology and Transplantation.

—Peter Farley

BRAIN DATA ON THE INTERNET

In an effort to help neuroscientists quickly find the latest information about the brain, the National Institutes of Health has established a consortium to design a Neuroscience Information Framework (NIF). The consortium includes scientists at Yale, the California Institute of Technology, Weill Medical College of Cornell University, George Mason University and the University of California at San Diego.

The NIF will help guide scientists to resources on the Internet by identifying software tools and data, developing language to describe the resources and placing them in a Web-accessible database. "To use this information effectively, neuroscientists need to be able to locate the latest research results that are relevant to the particular behavior they are studying or neurological disease they are treating," said Gordon M. Shepherd, M.D., PH.D., professor of neuroscience and neurobiology and a member of the Yale team.

—J.C.

How to fix the broken telephone

Phone conversations are a major source of miscommunication between doctor and patient.

As soon as the words were out of her mouth, she regretted them: while returning phone calls for a colleague, Anna B. Reisman, M.D., assistant professor of medicine, told the woman who answered the call that her husband had tested positive for gonorrhea. Not only should Reisman have declined to share test results with a family member, but as it turned out, she had misread the patient's chart. The family accepted Reisman's apology, but she'll never forget her indiscretion, and in the seven years that have passed

she's often asked herself how it could have been avoided.

Communication failures have been shown to play a key role in medical mishaps; telephone encounters, which account for 25 percent of interactions between physicians and patients, are particularly tricky. There are no visual cues to tell the physician how the patient is feeling, how he or she is reacting to a diagnosis or whether the patient can speak freely—all of which can set the stage for preventable errors.

In a paper published in the October issue of the *Journal of General Internal Medicine*, Reisman and co-author Karen E. Brown, M.D., assistant professor of medicine, outlined scenarios in which communication errors commonly occur, providing strategies to minimize mistakes. The scenarios involve sensitive test results, requests for narcotics, patients who are unwell but not sick enough for the emergency room, late-night calls, communicating with unintelligible patients and calls from patients' family members. In one scenario, a patient calls his physician in the middle of the night with back pain. Irritated at being awakened for a seemingly petty concern, the doctor terminates the call before the patient can explain that his symptoms include chest pain; the patient ends up hospitalized with a mild heart attack. In this situation, Reisman and Brown discuss the importance of careful questioning and suggest ways of drawing out hidden concerns. They advise giving the patient time to describe the chief complaint before interrupting, asking the patient why he or she is calling at that time and finding out if there is anything else the patient wants to commu-

nicate. In another scenario regarding sensitive test results, the strategies include scheduling an office visit (which can later be cancelled) when ordering tests that might have significant results; ensuring that patients can speak freely if the test findings are given over the phone; and not leaving results with family members or recorded on an answering machine. (Since the passage of the Health Insurance Portability and Accountability Act in 1996, all hospital staff have received training in protecting patient confidentiality.)

Physicians assess patients by observing aspects of their appearance, but the opportunity for visual inspection is missing in phone encounters. Improving phone skills can help doctors fill in some of that information. "Better communication improves doctor-patient relationships, decreases lawsuits and improves outcomes," said Reisman.

Despite advances in other communication technologies, the telephone will continue to play a major role in doctor-patient relationships, yet according to a 1995 survey, telephone medicine is taught in only 6 percent of residency programs. Reisman began teaching it to residents and physicians when she noticed how frequently residents talked about mistakes they had made when dealing with patients over the phone. By teaching the best way to handle telephone encounters, she hopes to help others avoid mistakes similar to the one she made almost a decade ago.

(For a different view of the clinical use of phones, see "Cell Phones Reduce Errors" on the next page.)

—Jill Max



Study finds sleep apnea is a major risk factor for stroke and death

Although previous studies have suggested links between sleep apnea and stroke, it was never clear whether the increased risk of stroke was related to such other factors as hypertension or diabetes. Now, in a study published in *The New England Journal of Medicine* in November, a Yale team has found that, regardless of other factors, sleep apnea can put people at risk for stroke—the third leading cause of death in the developed world.

“Our study shows that sleep apnea doubles the risk for development of stroke and death, and severe sleep apnea more than triples the risk,” said H. Klar Yaggi, M.D., assistant professor of medicine and principal investigator of the study. “We know that this risk was independent of other risk factors, including high blood pressure.”

As many as one in five adults in the United States suffer from sleep apnea, which causes them to stop breathing temporarily while they sleep. Their bed partners may notice such symptoms as loud snoring, gasping or pauses in breathing. Men are more at risk for sleep apnea than women; obesity is also a risk factor.

The new study, conducted between January 1997 and December 2003, enrolled 1,022 patients over the age of 50 who had gone to the Yale Center for Sleep Medicine for treatment. About 68 percent, 697 patients, had been diagnosed with obstructive sleep apnea syndrome. Hypertension, diabetes and obesity were more prevalent in this group. The mean apnea-hypopnea



Klar Yaggi found that sleep apnea doubles the risk for stroke and death and severe sleep apnea triples the risk.

index—the number of episodes of breathing cessation per hour—of those with the syndrome was 35. Those in a comparison group who did not have obstructive sleep apnea syndrome had a mean index of 2.

An unadjusted analysis found an association between obstructive sleep apnea syndrome and stroke or death from other causes. Age and diabetes, for example, were significant factors. But even after adjusting for age, sex, race, smoking, alcohol consumption and diabetes or cardiovascular disease, the study still found a significant link between sleep apnea and stroke or death. Only 16 in the comparison group suffered stroke or death, but 72 patients with obstructive sleep apnea syndrome had a stroke or died.

The study was supported by the National Institutes of Health, the Department of Veterans Affairs and the Yale Center for Sleep Medicine.

—John Curtis

PESTICIDE LINKED TO INFERTILITY

A common pesticide may interfere with the reproductive tract, leading to reduced fertility in women, according to Yale researchers.

In an article published in *Endocrinology* last August, the researchers reported that in studies in mice and in human tissue, methoxychlor (MXC), a substitute for the banned pesticide DDT, alters an estrogen-regulated gene in the reproductive tract and reduces the ability of the uterus to support embryo implantation. MXC, which is applied to crops, livestock, home gardens and pets, is one of several chemicals that can mimic the action of hormones and sometimes interfere with endocrine function.

“MXC has an adverse effect on these mice similar to that of DES, a synthetic estrogen,” said senior author Hugh S. Taylor, M.D., HS '92, associate professor in the Division of Reproductive Endocrinology and Infertility in the Department of Obstetrics, Gynecology and Reproductive Sciences.

“Female offspring of women exposed to DES were more likely to have an abnormally shaped cervix and were more prone to cancer of the vagina, miscarriages, early labor and other complications.”

—J.C.

CELL PHONES REDUCE ERRORS

Cell phones have long been banished from hospitals over fears of interference with medical devices. A study by a Yale anesthesiologist and colleagues, however, suggests that mobile phones speed communications and reduce medical errors. And digital phones rarely cause interference.

For a study published in *Anesthesia & Analgesia* in February, Keith J. Ruskin, M.D., associate professor of anesthesiology and neurosurgery, surveyed attendees at the 2003 meeting of the American Society of Anesthesiologists. Based on more than 4,000 responses, Ruskin found that 65 percent of anesthesiologists relied on pagers to communicate and 17 percent used cell phones. Of those who used pagers, 45 percent reported delays in communications. Only 31 percent of those who relied on cell phones reported delays.

—J.C.



In separate studies, Matthew State and Jeffrey Gruen discovered links among genetic mutations, brain development and disease.

Two Yale teams among *Science* Top 10 for 2005

Genetic mutations linked to brain development and disease were among last year's leading discoveries.

Two findings by Yale scientists have been included in *Science* magazine's list of the 10 leading scientific breakthroughs of 2005. The teams found evidence that both Tourette syndrome (TS) and dyslexia could stem from genetic defects linked to brain development. Their work was among research cited under the category "Miswiring the Brain." Although the article did not name specific scientists or institutions, it cited "clues about the mechanisms of diverse disorders including schizophrenia, Tourette syndrome, and dyslexia. A common theme seems to be emerging: Many of the genes involved appear to play a role in brain development."

Matthew W. State, M.D., PH.D. '01, the Harris Assistant Professor of Child Psychiatry and assistant professor of genetics, and the senior author of a report in the October 14 issue of *Science*, led the team that identified for the first time a genetic mutation associated with TS. The gene, which contributes to neuronal growth and communication, accounts for less than 2 percent of TS cases, but its discovery after years of searching offers the best chance yet to penetrate this socially debilitating disease. How the mutations participate with other genetic and environmental factors to increase risk for the disease is unknown. "We hope the clues this gene will give us will have widespread ramifications for

understanding the basic biology of this disorder," said State.

In its search for "that one unusual patient who would lead us to a gene," State's team found a child, diagnosed with TS and attention deficit hyperactivity disorder, who had a telltale break on chromosome 13. That clue led researchers to the nearby *SLITRK1* (*Slit* and *Trk*-like family member 1) gene, which had already been recognized to be active in the developing brains of rodents and to function in neuron growth. When they analyzed the gene from 174 people with TS, they found three individuals with mutations. No mutations of any kind were found in several hundred unaffected people, providing strong evidence that *SLITRK1* was contributing to the disease. Studying *SLITRK1* gives a starting point, said State, who likened their discovery to a string the researchers can now pull on to start to unravel the rest of the disease.

Another team at the School of Medicine found a genetic link to dyslexia, the reading disorder that affects millions of children and adults. A mutated version of a gene, located on chromosome 6 and called *DCDC2*, disrupts the formation of brain circuits that make reading possible. The findings deepen the "understanding of how the reading process works on a molecular level," said Jeffrey R. Gruen, M.D., HS '84, FW '88, associate professor of pediatrics and lead author of the study published in a special issue of *Proceedings of the National Academy of Sciences* in November.

In a study of DNA markers in 153 dyslexic families, Gruen's team found that up to 20 percent of cases of dyslexia are due to defects in the *DCDC2* gene. In the mutated version of the gene, a large regulatory region is deleted. Locating this gene explains, in part, why dyslexia occurs and could lead to early and more accurate diagnoses and more effective educational programs for dyslexic children.

—Pat McCaffrey

New twist on experiment unleashes the brain's potential for healing

When we pour concrete for a sidewalk or foundation, we want the material to be as fluid as possible, so that it will easily assume the shape we have in mind. But for our structure to be durable and useful, we want the concrete to harden—quickly.

The brain's early development is a similarly delicate balancing act between malleability and permanence. The areas of an infant's cerebral cortex devoted to sensory systems are highly plastic, so that cortical circuits can be efficiently sculpted in response to the sights, sounds and smells that make up the baby's world. But as soon as a baby has had enough time to acquire adequate sensory experience—a developmental window known as the "critical period"—neural circuits become hard-wired.

Fixed neural circuits ensure that cortical function is stable and reliable, but stability comes at a cost: if the brain or spinal cord is damaged by trauma,

disease or stroke, it can rarely repair itself well enough to restore function.

How the brain shuts the door on plasticity and how that process might be blocked to regenerate or repair neural circuits are the focus of the laboratory of Stephen M. Strittmatter, M.D., PH.D., the Vincent Coates Professor of Neurology.

In 2000, Strittmatter identified a protein called Nogo that suppresses self-repair in damaged axons. In order to establish whether Nogo shuts down plasticity more generally, Strittmatter and Nigel W. Daw, PH.D., professor of ophthalmology and visual science, married genetic techniques with a classic experiment devised by Nobel prize-winning neurobiologists David H. Hubel, M.D., and Torsten N. Wiesel, M.D., in the early 1960s.

Normally the visual cortex is divided equally between inputs from each eye into regions known as ocular dominance columns, but Hubel and Wiesel showed that if one of an animal's eyes is kept shut during the highly plastic critical period, the active eye's inputs will appropriate a larger share of the visual region, leaving vision in the other eye irreversibly impaired. However, as reported in the September 30 issue of *Science*, when Strittmatter, Daw and postdoctoral fellows Aaron W. McGee, PH.D., and Yupeng Yang, PH.D., performed the same experiment with mice specially bred to lack a functional Nogo receptor, the cortex remained plastic after the critical period, and an active eye could usurp cortical real estate from a deprived eye well into adulthood.

Encouraged by these and other results, Strittmatter is searching for Nogo blockers that he hopes will revive the capacity for plasticity, and healing, of the damaged or diseased brain and spinal cord. "Limited nerve cell regeneration and plasticity are central to a range of neurological disorders," he said, "including stroke, head trauma, multiple sclerosis and neurodegenerative disease."

—Peter Farley

PROTECTION AGAINST MAD COW

In 1996, during an epidemic of mad cow disease—bovine spongiform encephalopathy—in British cattle, epidemiologists predicted that up to 100,000 people could contract variant Creutzfeldt-Jakob disease (vCJD), a rapidly progressing, invariably fatal neurodegenerative condition, from infected beef. But that nightmarish scenario has not yet come to pass: 10 years later, only 151 cases of vCJD have been verified.

Laura M. Manuelidis, M.D. '67, HS '70, FW '70, professor and chief of surgery (neuropathology), may have discerned why. Manuelidis and colleagues reported in *Science* in October that exposure to less-virulent strains of CJD may protect against infection with the newly evolved bovine strain. The team found that when neuronal cell cultures were infected with either a weak or sporadic form of CJD, or with agents that cause sheep scrapie, a disease similar to CJD, they resisted infection by the more-virulent strain.

—P.F.

TASTE AND SMELL—THE NOSE KNOWS

Although our taste buds distinguish sweet, sour, salty, savory and bitter, flavor arises from a combination of tastes with odors that enter our nasal passages through the back of the mouth. These "retronasal" odors get special treatment from the brain, according to a new study led by Dana Small, M.Sc., PH.D., assistant professor of surgery (otolaryngology) and psychology at Yale and an assistant fellow at the John B. Pierce Laboratory.

In a report published in *Neuron* in August, Small and colleagues at Yale and in Germany inserted tubes that pumped odors such as chocolate into subjects' noses, either to the front of the nostrils or to the back of the nasal cavity. They found that a single odor could activate different brain regions, depending on the route it traveled. Odors presented retronasally activated brain areas devoted to the mouth, which Small said is "evidence of the existence of distinct olfactory subsystems"—one specialized for sensing objects at a distance, the other for sensing objects in the mouth.

—P.F.



Stephen Strittmatter and colleagues used a fluorescent green marker to stain myelin in the cortex. Myelin contains the Nogo protein, which prevents the repair of damaged neural circuits. In recent experiments they found that knocking out the Nogo receptor permitted increased plasticity and healing.

AARON MCGEE

Steven Marans draws on clinical research and his own experiences to explore the fundamental fears all people share.

Coping with life's everyday fears

Drawing lessons from trauma, author offers parents advice on a child's anxieties, large and small.

It was 3 a.m. on a summer night in 2004 when the sound of a pager awoke psychoanalyst Steven R. Marans, M.S.W., PH.D. The New Haven police were summoning him to a home where three children had witnessed a murder. Along with colleagues in the city's Child Development-Community Policing Program (which Marans founded with the late Donald J. Cohen, M.D. '66, in 1991), Marans invited the children to draw pictures and to talk about any aspects of the event they wished to discuss.

As a nationally known expert on children facing severe trauma, Marans spends much of his time helping children and those who care for them to cope with major upheavals—domestic violence, school shootings, the 9/11 attacks and such natural disasters as Hurricane Katrina. Since 2000 he has also directed the National Center for Children Exposed to Violence, a federal program based on Yale's partnership with the New Haven police.

Now Marans, professor of child psychiatry and psychiatry at the Yale Child Study Center and in the department of psychiatry, has applied his insights to writing a guide for parents that explores the day-to-day challenges of growing up. In his first book for a general audience, *Listening to Fear: Helping Kids Cope, From Nightmares to the Nightly News*, Marans suggests that children's reactions to stress have a common source. Whether the stressor is as extreme as witnessing a murder or as ordinary as coping with teasing, the common source is fear.

Marans, who has been trained in both child and adult psychoanalysis, shows in his book how fear enters into everyday events with a description of a supermarket tantrum by his toddler son (now a college student). For the child, fear played a role—perhaps he feared his lack of competence when his father had to lift him to reach a container of sour cream. Most likely the child also scared himself with his outburst. But the incident stirred Marans' own fears: loss of control, loss of his self-image as someone skilled in understanding children—and loss of face as he imagined onlookers judging him a bad parent. Those fears Marans could explain rationally.



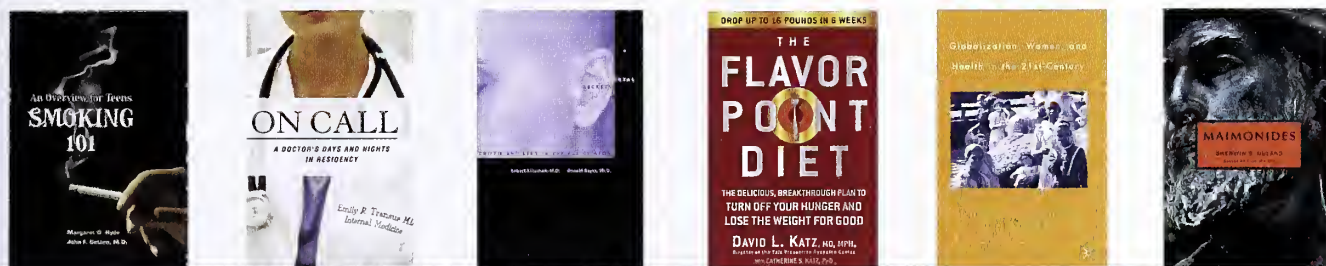
Marans says that children's fears also evoke their parents' suppressed fears, fears that stem from the normal course of development and from their own childhood experiences. "We desperately want to wave the proverbial magic wand and wave our children's feelings away, not only because we don't like to see our children unhappy but also because it stirs up our own feelings—feelings that we're reminded of by our kids' experiences," said Marans.

Drawing on clinical research and his own experience, Marans said all people share five fundamental fears: loss of life (of loved ones and of oneself); loss of the love of others and for ourselves; bodily harm; losing control of our feelings, impulses or thoughts; and losing the assumed predictability of daily life. By distinguishing our own fears from our child's, Marans said, we become better parents. We need to listen, not only to words but also to behavior, which may be the child's only means of expressing distress.

"My interest in extreme situations is an extension of the concern that I always have: how we use our understanding of human behavior and human development as a way of illuminating people's experience," said Marans during an interview at the Child Study Center. "What I hope the book does is remind us that the worst of our fears, fears that can reach overwhelming or dramatic proportions, are elaborations of the basic fears and anxieties that are part of who we are as human beings. Discovering that there is, in fact, sense to what we feel and how we act can be tremendously reassuring."

—Cathy Shufro

Bookshelf is a column focusing on matters related to books and authors at the School of Medicine. Send ideas to Cathy Shufro at cathy.shufro@yale.edu.



Smoking 101:

An Overview for Teens

by Margaret O. Hyde and John F. Setaro, M.D., HS '86, FW '92, associate professor of medicine (cardiology) (Twenty-First Century Books) This book provides information that will help teenagers considering whether to try cigarettes. For teens who already smoke, the authors describe programs and techniques for quitting and list websites of organizations that can help.

On Call: A Doctor's Days and Nights in Residency

by Emily R. Transue, M.D. (St. Martin's Press) While a resident at the University of Washington, Transue, Yale College Class of 1992, wrote about her patients as a way to guard against burnout and share her experiences with friends and family. This collection of stories conveys the atmosphere of overwork, exhaustion and insecurity in which a resident works, as well as Transue's compassion for her patients.

Mortal Secrets: Truth and Lies in the Age of AIDS

by Robert Klitzman, M.D. '85, and Ronald Bayer, PH.D. (The Johns Hopkins University Press) The authors provide a portrait of moral, social and psychological decision making by drawing on interviews and testimonies from more than 70 gay men and women, intravenous drug users, sex workers, bisexual men and heterosexual men and women. For those who are HIV-positive, decisions about disclosure of their diagnosis make them confront intimate questions about truth, lies, sex and trust.

Shields' Textbook of Glaucoma

edited by R. Rand Allingham, M.D., Karim F. Damji, M.D., Sharon F. Freedman, M.D., Sayoko E. Moroi, M.D., PH.D., George Shafranov, M.D., associate professor of ophthalmology and visual science, and M. Bruce Shields, M.D., the Marvin L. Sears Professor of Ophthalmology and Visual Science (Lippincott Williams & Wilkins) Readers will find updated information on the cellular and molecular biology of the eye, molecular genetics of glaucoma and congenital and developmental glaucomas. The book also describes management of glaucoma and approaches to treatment. Each chapter includes summaries of key points.

Psychological Aspects of Reconstructive and Cosmetic Plastic Surgery: Clinical, Empirical and Ethical Perspectives

edited by David B. Sarwer, PH.D., Thomas Pruzinsky, PH.D., Thomas F. Cash, PH.D., Robert M. Goldwyn, M.D., John A. Persing, M.D., professor of surgery (plastic) and neurosurgery, and Linton A. Whitaker, M.D. (Lippincott Williams & Wilkins) This volume examines the relationships among physical appearance, body image and psychosocial functioning. The authors detail the psychological implications of specific disfigurements and of reconstructive procedures, and discuss bioethical, professional and legal issues.

The Flavor Point Diet:

The Delicious, Breakthrough Plan to Turn Off Your Hunger and Lose the Weight for Good

by David L. Katz, M.D., M.P.H. '93, associate clinical professor of public health, and Catherine S. Katz, PH.D. (Rodale Books) This book introduces readers to the Flavor Point Diet and provides menu plans and recipes. By combining foods selected by flavor, the regimen "tricks the brain into being satisfied all day."

Globalization, Women, and Health in the 21st Century

by Ilona S. Kickbusch, PH.D., former professor of public health, Kari A. Hartwig, DR.P.H., assistant clinical professor of public health, and Justin M. List, M.DIV. '04 (Palgrave Macmillan) This book explores the complex set of interdependencies among gender, health and globalization.

The Psychotherapist's Own Psychotherapy: Patient and Clinician Perspectives

edited by Jesse D. Geller, PH.D., associate clinical professor of psychiatry, John C. Norcross, PH.D., and David E. Orlinsky, PH.D. (Oxford University Press) The first-person narratives, clinical wisdom and research findings gathered in this book offer guidance for providing effective treatments to patients who are also therapists.

Medical Complications During Pregnancy, 6th ed.

edited by Gerard N. Burrow, M.D. '58, HS '66, the David Paige Smith Professor Emeritus of Medicine and dean emeritus, Thomas P. Duffy, M.D., professor of medicine (hematology), and

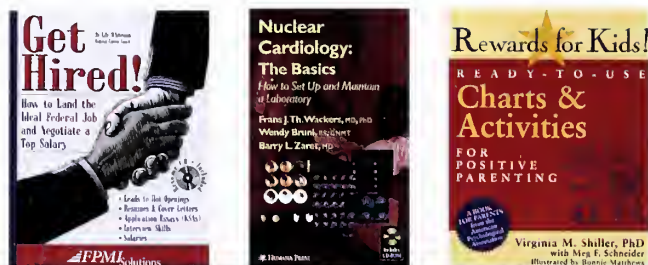
Joshua A. Copel, M.D., FW '85, professor of obstetrics, gynecology and reproductive sciences and of pediatrics (W.B. Saunders) This reference book presents multidisciplinary coverage of the full spectrum of complications associated with pregnancy. Postpartum depression and bioethics are two of the topics covered.

Foundations of Anesthesia: Basic Science and Clinical Practice, 2nd ed.

edited by Hugh C. Hemmings Jr., PH.D. '86, M.D. '87, and Philip M. Hopkins, M.D. (Elsevier) International experts provide complete coverage of basic and clinical science in anesthesiology, emphasizing the principles and clinical applications of molecular and cell biology, physiology, pharmacology and physics and measurement.

Maimonides

by Sherwin B. Nuland, M.D. '55, HS '61 (Schocken Books) Maimonides was a physician, a Torah scholar, a community leader and a philosopher who attempted to reconcile scientific knowledge with faith in God. He was a Jew living in a Muslim world, a rationalist living in a time of superstition. Nuland gives us a portrait of Maimonides that makes his life, his times and his thought accessible to the general reader.



Get Hired! How to Land the Ideal Federal Job and Negotiate a Top Salary

by Lily Whiteman, M.P.H. '90 (FPMI Solutions) This book, based on the experiences of people who found federal jobs, provides tips for breaking into the federal job market—from entry-level to executive positions. The author provides strategies for finding domestic and overseas openings, lists the latest federal jobs websites and offers tips for mastering online applications.

Reconceiving the Gene: Seymour Benzer's Adventures in Phage Genetics

by the late Frederic L. Holmes, PH.D., the Avalon Professor of the History of Medicine and chair of the Section of the History of Medicine, and edited by William C. Summers, M.D., PH.D., professor of therapeutic radiology and of molecular biophysics and biochemistry (Yale University Press) More than any other individual, biologist Seymour Benzer is considered to have led geneticists from the classical gene into the molecular age. Drawing on Benzer's record of his experiments, correspondence and published sources, this book reconstructs how the former physicist initiated his work in phage biology and achieved his landmark investigation.

Nuclear Cardiology, the Basics: How to Set Up and Maintain a Laboratory

by Frans J.Th. Wackers, M.D., PH.D., professor of diagnostic radiology and medicine, Wendy Bruni, and Barry L. Zaret, M.D., the Robert W. Berliner Professor of Medicine and professor of diagnostic radiology (Humana Press) This guide offers a concise, action-oriented plan for solving the many practical and technical problems involved in establishing and running a nuclear cardiology lab. The authors answer basic questions about purchasing equipment and determining space requirements.

Rewards for Kids! Ready-to-Use Charts & Activities for Positive Parenting

by Virginia M. Shiller, PH.D., lecturer in the Child Study Center, and Meg F. Schneider (Magination Press) This book shows how to motivate children to improve their behavior and fulfill their responsibilities, using a variety of child-friendly sticker charts and other tools. The authors teach parents positive techniques for helping children to overcome such common behavior problems as bedtime procrastination and fighting with siblings.

The descriptions above are based on information from the publishers.

SEND NOTICES OF NEW BOOKS TO Cheryl Violante, Yale Medicine, P.O. Box 7612, New Haven, CT 06519-0612, or via e-mail to cheryl.violante@yale.edu

Consortium seeks to boost minority presence in health information professions

A senior at Hill Regional Career Magnet High School in New Haven, Jordon Thomas was impressed when he first set foot in the Cushing/Whitney Medical Library last summer. "I didn't know there were so many resources that were right in front of me," said Thomas, who attended a science program sponsored by the School of Medicine.

Thomas is just the type of student that Charles J. Greenberg, M.L.S., M.ED., coordinator of medical library curriculum and research support, would like to attract to the health sciences information professions: a college-bound minority student who might consider becoming a medical librarian or health information specialist. (As it turns out, Thomas, who is African-American, plans to be a pharmacist.) Greenberg is the project coordinator for a newly formed consortium of eight university medical libraries that is trying to interest minority students in careers in medical librarianship. Nancy K. Roderer, M.L.S., former director (1992-1999) of Yale's medical library and now director of the William H. Welch Medical Library at Johns Hopkins, is the principal investigator. Funded with a three-year, \$640,000 matching grant from the federal Institute of Museum and Library Services, the group comprises Yale, Georgetown University, Houston Academy of Medicine, Howard University, the University of Colorado at Denver, Johns Hopkins University, the University of Tennessee and Washington University in St. Louis. Currently, 9 percent of medical librarians are members of minority groups.

The effort to interest minority students is part of a broader attempt to recruit health care professionals who reflect the ethnic and racial diversity of their patients. "Health care providers are very concerned with cultural competence," said Greenberg. "We want to become part of that mosaic of health careers." The medical librarianship project is just in the planning stage, but libraries in the group plan to sponsor tours, internships and other outreach programs.

The group's task in part is to replace the image of a dowdy librarian with a more up-to-date view of a computer-savvy "information specialist."

Yale's medical library has been "at the forefront of the university's partnerships with the New Haven public schools," said Claudia R. Merson, director of public school partnerships at the Office of New Haven and State Affairs. For instance, Yale medical librarians taught Internet skills to Career High School teachers and administrators in the mid-1990s. "This is another opportunity," said Merson. "There's been so much exposure to health professions, but librarianship has not been one of them. It's new and exciting, and it looks like it's going to be cool."

The project's website is <http://www.bioinfo-career.org/>.

—Cathy Shufro

In Circulation is a column focusing on activities at the Cushing/Whitney Medical Library. Send ideas to Cathy Shufro at cathy.shufro@yale.edu.



Paul K. Carlton Jr.

Emergency care in the wake of Katrina

If there was a good news story about Hurricane Katrina, it was the medical response to the disaster, said Paul K. Carlton Jr., M.D., director of the Office of Homeland Security of the Texas A&M University System Health Science Center. Speaking at the Yale New Haven International Congress on Disaster Medicine and Emergency Management in September, Carlton described how emergency "surge" hospitals mobilized to handle thousands of patients in Baton Rouge.

"Your worst nightmare is to lose an entire medical network, and that is what happened in Katrina," said Carlton, a proponent of the surge concept, in which hospitals expand facilities or open new ones in emergencies. Within days, he said, health and disaster teams had set up four surge hospitals in Baton Rouge, including one at a former Kmart store that had been closed for 10 years. "It was filthy," Carlton said. Crews found portable air-conditioning units, got power to the building, bought portable toilets and converted the big-box store into a 1,000-bed hospital.

Driving the medical teams, Carlton said, was a basic principle: "We will not break trust with our patients."

—John Curtis

Judah Folkman

Bright future for a roller-coaster compound

In 1998, Endostatin, a protein that inhibits blood vessel growth, was touted as a silver bullet for cancer after tests in mice showed it killed tumors by cutting off their blood supply. But six years later, the future looked bleak: *Fortune* magazine said the angiogenesis inhibitor "failed dramatically" in clinical trials, and EntreMed, a Maryland biotech company, abandoned the drug in 2004 after flirting with bankruptcy.

But Endostatin is not dead yet, according to its creator, Judah Folkman, M.D., who spoke at Yale in October. Folkman, a Harvard researcher, said both reports exaggerated the reality. His work led to FDA approval in 2004 of another angiogenesis drug, Avastin, which is expected to reach \$6 billion in sales and may become the largest-selling anticancer drug in history.

Three weeks before Folkman's Yale talk, China approved an Endostatin product developed and tested by the Chinese biotech company Medgenn. A trial involving 493 late-stage lung cancer patients showed that its Endostar drug was effective, doubling survival time from three to six months when combined with chemotherapy. Folkman hopes the Chinese findings will revive the future of Endostatin in the American market. "It's had a tough life," he said, "but it's been resuscitated."

—Michael Fitzsiousa

Walter J. Freeman

A pioneering lobotomist's mixed legacy

When he began his biography of Walter J. Freeman, M.D., a Yale College graduate who pioneered lobotomy in the United States, journalist Jack El-Hai expected he would be writing about "a monster."

The truth was more complicated, said El-Hai, author of *The Lobotomist: A Maverick Medical Genius and His Tragic Quest to Rid the World of Mental Illness*, speaking at a master's tea at Yale in November. Psychiatrists embraced the crude surgery that severed neural pathways between the frontal lobes and the thalamus, El-Hai argued, because until the advent of Thorazine in 1954 they had few effective treatments for psychiatric illnesses. "They were willing to try something experimental, something desperate... because at least it held out some hope," said El-Hai.

From 1936 to 1967 roughly 40,000 patients underwent lobotomies nationwide, for conditions ranging from depression to schizophrenia. Freeman did 3,400 of them, including one on a sister of John F. Kennedy. Some patients felt better, some became disabled and 2 percent died.

Freeman, El-Hai noted, "was one of the few advocates of a biological orientation for psychiatry. That is his most positive legacy today, if you can find one."

—C.S.

Dikembe Mutombo

NBA star makes a giant impact in his African homeland

As he walked through campus last September, Dikembe Mutombo, all-star center for the Houston Rockets, cut a somewhat startling figure. With an impeccably tailored deep-blue suit draped over his 7-foot, 2-inch frame, Mutombo towered over his hosts like a grade-school teacher minding charges on a field trip.

He came to Yale at the invitation of Anup Patel, a second-year medical student who had heard of the Dikembe Mutombo Foundation's humanitarian work in Mutombo's native Democratic Republic of Congo (DRC). Mutombo contributed \$10 million for the construction of a 300-bed hospital in the capital of Kinshasa, which will open in June to provide care to the city's poorest residents and to train its health professionals. Yale and the foundation are considering a partnership that would provide opportunities for medical students to travel to the DRC for clinical clerkships.

"I grew up poor and I never forgot where I came from," said Mutombo, in an address at Battell Chapel. "If I was going to do something that will carry my legacy, I wanted to make sure it was very good, that it will stop the suffering, that it will help the people that don't have a chance to go on a plane to go to South Africa or Europe to get treatment."

—Peter Farley



Harvey Cushing

the man, the surgeon and the father

By Peter Farley

A new biography of the pioneering neurosurgeon explores different facets of the man who revolutionized brain surgery.



Our operating room —

CUSHING/WHITNEY MEDICAL LIBRARY (2)

J. Michael Bliss, PH.D., author of a new biography of Harvey W. Cushing, M.D., assumed the lectern at the Hope Auditorium last October to face what a Catskills comic might call a tough crowd: Cushing's descendants and relatives, who had gathered to celebrate the renowned neurosurgeon's life and to plan for a permanent home at Yale for Cushing's rich collection of brain specimens, photographs, drawings and memorabilia.

But Bliss, a historian at the University of Toronto, proceeded without fear or favor as he discussed his book, *Harvey Cushing: A Life in Surgery*, and wasted no words in raising an issue of interest to those with a personal connection to the notoriously demanding Cushing. "There's vigorous debate about Cushing's professional motives and his professional personality, and this is the kind of thing we have to talk about so long after his death," Bliss declared. "The question is whether or not he was an egotistical, hard-driving, selfish, mean son-of-a-bitch."

Perhaps to smooth the way for that question, Bliss first emphasized that Cushing, an 1891 Yale College graduate and one of the most lauded figures in the history of medicine, truly was as great as his admirers would have it. In diligence, innovation and pure skill, Bliss said, Cushing—father of modern neurosurgery, artist, Pulitzer Prize-winning biographer of Sir William Osler and more—had no equal. Before Cushing, patients routinely bled to death during intracranial surgery, which had a mortality rate approaching 50 percent. Thanks to his introduction of rigid haemostasis, asepsis, electrocoagulation and other procedures, mortality rates plummeted to 10 percent.

In his professional life Cushing was a "tough hombre" who "reduced nurses to tears and residents to nervous breakdowns with withering scorn and sarcasm," Bliss said. Cushing's punishing schedule—including regular 98-hour weeks—exacted a toll on his wife and children, who "found it difficult to relate

to their stern Victorian father, who disapproved of jazz, the movies, fashionable dress, telephone calls, boyfriends, women in medicine, women smoking—probably women at college—and young men who did not attend to their studies and the need to get on with qualifying for Yale."

His patients, however, knew another Cushing. "His bedside manner was absolutely wonderful; his dedication to his patients absolutely boundless," Bliss said.

Cushing's reaction to his son Bill's death poignantly captured his complex sense of duty. While Cushing was teaching surgery at Harvard Medical School and the Peter Bent Brigham Hospital in Boston, Bill died in an automobile accident after a night celebrating the end of his junior year at Yale. Cushing "called [his wife] Kate to tell her, then carried out a scheduled operation, which was a success, then told his team about the family tragedy and left for Connecticut to claim his son's body."

Though Cushing spent almost his entire professional life at Johns Hopkins and at Harvard, his undergraduate years at Yale College were so formative and important to him that he returned to Yale at the end of his surgical career to be Sterling Professor of Neurology and director of studies in the History of Medicine. There could be no more appropriate place than the School of Medicine to house the Cushing Collection, Bliss said.

"He was one of Yale's most illustrious graduates, and the preservation of his work and legacy at Yale—his books, his papers, and now his wonderful collection of patient photographs and specimens—is a fitting aspect of the university's service to generations past, present and future. Although Harvey Cushing learned a lot and did a lot at Johns Hopkins and at Peter Bent Brigham," Bliss said, "Yale was his alpha and his omega."

Peter Farley is a contributing editor of *Yale Medicine* and the managing editor of the medical school's bimonthly newsletter, *Medicine@Yale*.



OPPOSITE TOP Harvey Cushing in 1907 at his desk at Johns Hopkins, six years after he began his residency under the tutelage of surgeon William Stewart Halsted. While at Hopkins, Cushing rose to fame as a neurosurgeon and an expert in the pituitary gland.

OPPOSITE BOTTOM An undated photo of a Cushing operating room. Cushing's innovations in intracranial surgery reduced mortality rates from about 50 percent to 10 percent.

ABOVE Throughout his career Cushing kept meticulous records of his cases, including photographs of his patients, such as this one showing a surgical incision. He also made detailed drawings of the brain. His collection of notes, microscopic slides, brain specimens and photographs are now known as the Cushing Brain Tumor Registry. The knowledge gleaned from the registry revolutionized the practice of neurosurgery.

CUSHING BRAIN TUMOR REGISTRY (2)

Yale connections around the world

A medical student's summer research journey becomes a Yale—and family—reunion like no other.

By Jill Max



Medical student Tamara Lazic traveled to Italy last summer for a research project with her advisor, interventional radiologist Robert White. During her stay she was reunited with her mother, who lives in Serbia, and introduced to a world of Yale connections.

When Tamara Lazic, now a second-year student at the School of Medicine, sought to combine a passion for languages with research for her thesis, she had no idea the project would take her halfway around the world to work in a clinic where a Yale physician collaborating with a former Yale fellow would perform a life-changing procedure on her mother.

A native of Belgrade, Serbia, Lazic traveled to Los Angeles in 1999 to live with her father, and in 2004 came to New Haven, after graduating from UCLA with a degree in physiological science. Like many students at the School of Medicine, she wanted to begin research for her thesis during the summer between her first and second years. But Lazic, who speaks Serbo-Croatian, English, Spanish and some Russian, also wanted to learn another language. She set her sights on Italy, which had the added bonus of being located just across the Adriatic Sea from her mother, a legal advisor in the Ministry of Internal Economic Relations of Serbia and Montenegro.

While researching overseas projects, Lazic came across the work of Robert I. White Jr., M.D., professor of diagnostic radiology and director of the Yale Vascular Malformation Center. An interventional radiologist, White travels widely to treat patients and educate physicians about hereditary hemorrhagic telangiectasia (HHT), a vascular disorder. Patients with HHT, also called Osler-Weber-Rendu syndrome, lack the capillaries that normally form between arteries and veins. This lack creates fragile sites that can rupture and bleed due to the flow of high-pressure arterial blood directly into veins. About 95 percent of people with HHT have recurrent nosebleeds, but lesions and malformations can occur in many parts of the body. Defects in smaller blood vessels, such as those inside the nose or on the skin, are known as telangiectases, while those in the larger blood vessels in the liver, lungs, brain and gastrointestinal tract are called arteriovenous malformations (AVMs). HHT affects approximately one person in 5,000, involves multiple organs and often goes undiagnosed. White has been on a mission to understand and treat HHT since 1990, when he

helped found the Hereditary Hemorrhagic Telangiectasia Foundation International (www.hht.org). Since then he has been instrumental in establishing 20 HHT Centers of Excellence in the United States, Europe and Japan. "For every 100 patients with HHT, 40 have lung or brain malformations, and half of those will be disabled or die prematurely from something that can be fixed," he said. Treatment usually involves embolization, a minimally invasive procedure in which the blood supply to the abnormal blood vessels is cut off.

White's enthusiasm for the HHT cause is contagious, and Lazic quickly signed on to spend last summer at the HHT center at the University of Bari in southern Italy, where she did research on diffuse pulmonary AVMs, the most severe form of the disease, in which multiple AVMs form in one or both lungs. White has close ties to the Bari center, which he visits twice a year to help treat patients. The center was established thanks to HHT patient Nicola Signorile, whom White met at a conference in Denmark in 1999. Signorile, a retired accountant, had suffered severe nosebleeds for 30 years before being diagnosed with HHT in 1997, but had been unable to find a physician to treat him. White encouraged him to seek out a physician in Italy who would be interested in learning more about diagnosing and treating the disease. Signorile's search led him to Carlo Sabbà, M.D., F.W. '90, a professor of medicine at the University of Bari, who had completed a two-year hepatology fellowship at Yale in 1990. Signorile introduced Sabbà to White at a conference in Toronto in 2000 and Sabbà was hooked: with the help of university President Giovanni Girone, a college classmate of Signorile, the University of Bari opened the Interdepartmental HHT Center in 2001 with Sabbà as its director.

Four years after it opened, the Bari center now treats 300 families from all over Italy and southern Europe. "Our center came about as Yale's offspring, but is now growing into a beautiful adolescent," said Sabbà. White has helped train doctors there to repair AVMs and continues to assist in complex cases during his regular visits. In 2005 he convinced Signorile, who had suffered a cardiac arrest following a severe nosebleed in which he lost two liters of blood, to come to Yale for a septal dermoplasty, a procedure perfected by Yale HHT team member Douglas A. Ross, M.D., associate professor of surgery (otolaryngology). Last June Signorile underwent the procedure, which involves replacing the lining of the nose with a skin graft from the thigh. He couldn't be happier with the results. "It was

extraordinary," he said. "I want everyone to know, because people are afraid of this operation, especially in Italy."

Meanwhile, Tamara Lazic's mother, Vesna Lazic, 51, had a different problem. She had been suffering from pelvic pain and bleeding so severe that it was sapping her energy and making her daily activities difficult. When Lazic showed White her mother's medical records, he suspected, correctly, uterine fibroids. In his travels, White also teaches uterine-fibroid embolization, a procedure similar to the one used to treat AVMs, in which the fibroid's blood supply is cut off, literally starving the tumor to death. Viewing Vesna Lazic's case as both a teaching opportunity (the procedure is unavailable in Serbia and had not been done at Bari) and a chance to help both her and her daughter, he offered to perform the procedure in Bari. Sabbà and Girone immediately arranged to accept Vesna Lazic as a patient at no charge, but the next obstacle was getting her to Italy. It normally takes a month to obtain a visa to enter Italy from Serbia, but White had to leave the country in just a few days. Girone used his contacts at the Italian embassy in Belgrade to prevail upon authorities to speed the process.

Lazic and her mother see each other only once a year, and were overjoyed to be reunited and to resolve Vesna Lazic's medical problems. Vesna Lazic arrived in Bari in August; White successfully performed the embolization and taught doctors there how to do the procedure. "It opened a lot of doors for them," said Lazic, who is grateful for the help she and her mother received.

Looking back, Lazic is amazed at the turn of events that led to her mother's uterine-fibroid embolization. As a Yale medical student, she traveled 3,000 miles for her thesis project, where she met a former Yale patient, worked with a Yale-trained specialist in a center whose existence was sparked by Yale research and saw "image-guided therapy" performed on her mother by a Yale physician. All these encounters were in a sense made possible by Sanford G. Bluestein, M.D. '46, a retired radiologist who is sponsoring Lazic's medical education through a scholarship fund he established in 1996. It's quite a journey for a young woman who grew up in war-torn Serbia and who sees the opportunity to attend Yale as a dream come true. "If you told me six years ago that I would end up at Yale," she said, "I wouldn't have believed you."

Jill Max is a freelance writer in Connecticut.



One in 10 human cancers starts with a viral infection, often the ubiquitous human papillomavirus. Yale scientists want to know why—and are hot on the trail of new vaccines and therapies to treat

the virus

behind the cancer



By Jennifer Kaylin

Illustrations by Yasuo Tanaka

Photographs by Terry Dagradi

More than 50 years ago, a young woman named Henrietta Lacks was diagnosed with cervical cancer. Despite surgery and aggressive radiation therapy, the cancer soon spread throughout her body, and on October 4, 1951, she died.

It was a cruel death for the 31-year-old mother of five, but Lacks' story didn't end there. George O. Gey, M.D., head of tissue culture at Johns Hopkins University, where Lacks was treated, had been searching, for research purposes, for a line of human cells that could live indefinitely outside the body. He got his wish when cells from Lacks' cancerous tumor were cultured. Just as they had done in her body, the cells multiplied ferociously in the lab, crawling up the sides of test tubes and consuming the medium around them.

An entire generation of the cells reproduced every 24 hours.

Referring to Lacks' cells, Gey declared at the time, "It is possible that, from a fundamental study such as this, we will be able to learn a way by which cancer can be completely wiped out." To this day, Lacks' cells, known as the HeLa cell line, are some of the most robust and rapidly growing cells known to science. They are still used by thousands of researchers around the world to decipher the complexities of cell biology, particularly as they apply to cancer.

At Yale, scientists are using the HeLa cell line to study, among other things, the human papillomavirus (HPV) that

causes the cervical cancer that killed Lacks. "Her legacy," says Daniel C. DiMaio, M.D., PH.D., the Waldemar Von Zedtwitz Professor of Genetics and professor of therapeutic radiology, "is that her cells are helping us unravel the pathogenesis of cervical cancer, so that some day we might be able to prevent and treat it. It's rather remarkable."

The field of human tumor virology is still a relatively new area of scientific inquiry. Although it has been known for nearly a century that viruses can cause tumors in animals, only in recent decades have human tumor viruses been identified. Researchers at Yale, among them I. George Miller, M.D., have contributed to our understanding of the mechanisms of viral tumorigenesis.

Miller, the John F. Enders Professor of Pediatrics and professor of epidemiology and of molecular biophysics and biochemistry, was the first to show that a human virus can cause tumors in primates. Experiments he conducted at Yale in the 1960s showed that the Epstein-Barr virus (EBV) could cause lymphoma in cotton-top marmosets. He also showed that the virus was very effective at changing normal human lymphocytes into cells with properties of cancer cells in culture.

More recently, DiMaio's lab demonstrated that cervical cancer cells need the viral proteins to grow, thus raising the possibility that the cancers can be treated with antiviral



drugs. DiMaio, Janet L. Brandsma, PH.D. '81, and others are currently working on a vaccine to treat patients with cervical cancer.

Besides these advances, Yale researchers who specialize in tumor virology believe their work could have wider applications, potentially expanding knowledge of a range of cancers and other illnesses and biological processes, such as cellular aging. "It will help us understand all cancers," says Brandsma, an associate professor of comparative medicine and pathology. "Most small mutations in cellular genes are very subtle, but with viral cancers, the viral genome in the cancer cell is foreign and easier to recognize. It's an excellent model."

Chickens, rabbits, warts and mice

More than 10 percent of all cancers in humans are strongly associated with infection by tumor viruses, and roughly 15 percent of all cancer deaths worldwide are caused by viruses. "It's a very important problem," DiMaio says. But he also sees tumor virology as a tremendous opportunity. "Once you know that a cancer is caused by a virus, you are far ahead of where you'd be for any other cancer, because you've identified the target, you've identified the cause and you have well-established ways to prevent or treat the disease that just don't exist for spontaneously arising tumors."

To say that certain viruses *cause* certain cancers can be misleading. You can't catch cancer from another person, and most people who are infected with HPV, for example, won't get cervical cancer. However, everyone who gets cervical cancer has the HPV infection. "Other things have to go wrong in order for the cancer to develop," DiMaio explains, "but the virus contributes in an essential way. If you prevent virus infection by vaccination, you don't get the cancer, and if you turn off the virus, the cancer can't grow."

HPV is the best-understood example of how a virus leads to cancer. Two things have to happen: First, viral gene products cause the cells to become genetically unstable and accumulate mutations that render cells unresponsive to

aspects of growth control and the immune response. Second, the viral oncogenes provide a sustained stimulus to cell growth.

The first clue that there was a viral link to certain cancers came in 1911. Using a virus found in chickens, F. Peyton Rous, M.D., a scientist at the Rockefeller Institute for Medical Research, showed that the chicken sarcoma could be induced in other chickens. "There was a lot of doubt about what applicability it had, if any, to human disease," says Miller. But in 1966 Rous shared the Nobel Prize in physiology or medicine for his research on the link between viruses and cancer, and the chicken virus became known as the Rous sarcoma virus.

Another important development, Miller says, came in the 1930s, when Richard Shope, M.D., one of Rous' collaborators and the father of the late Yale epidemiologist Robert E. Shope, M.D., HS '58, was out hunting with a friend. The friend mentioned that he'd seen rabbits with horns—actually giant warts. Shope asked his friend to send him some of the horns, which he then ground up, so he could isolate the virus causing the warts. When he injected the virus into other rabbits, they also grew horns. Interestingly, when New Zealand white rabbits were inoculated with the virus, they grew horns, but Shope couldn't recover the virus; in cottontail rabbits, the virus was retrievable. This discovery raised the question of viral latency, which scientists now know is intrinsic to the behavior and biology of tumor viruses. (Miller is currently researching latency as it relates to the Kaposi sarcoma virus. He's trying to determine what the suppressor mechanism is and why latent-state viral genomes are suppressed in the tumor cells and then periodically reactivated.)

In the early 1950s Ludwik Gross, M.D., head of cancer research at the Bronx (N.Y.) VA Hospital, opened the field of tumor virology in mammals with his discovery of what became known as the Gross mouse leukemia virus. Gross showed that a virus led to mouse leukemia and could be passed from one generation to the next.

Although these and other studies unequivocally showed that viruses can lead to tumors in animals, making



"When I arrived at Yale in 1983, people didn't think these viruses were important to cancer. At conferences the human papillomavirus was always the last talk of the meeting. Now it's taken center stage."

—Daniel DiMaio

the leap to human tumor viruses wasn't easy. Researchers encountered several obstacles. For starters, only a small percentage of people who are infected actually develop cancer; it takes more than a virus infection for a tumor to form; and other factors, such as immunosuppression or exposure to another carcinogen, must be present. Finally, it can take decades for symptoms to appear.

Despite these challenges, in 1965 the first bona fide example of a human tumor virus—EBV—was discovered in cells from Burkitt lymphoma. Since then scientists have identified six viruses that have been shown to play a role in human cancers.

HPVs are a family of small DNA viruses that typically cause benign warts. However, certain high-risk HPV types have been linked to a variety of carcinomas, the most prevalent being cervical cancer. HPV is also thought to play a role in other anogenital cancers, skin cancers and some head and neck tumors.

Hepatitis B virus and hepatitis C virus are genetically unrelated, but both can cause acute and chronic liver disease, which, under certain conditions, can progress to primary hepatocellular carcinoma. EBV is a herpes virus that can cause mononucleosis. However, EBV has also been linked to Burkitt lymphoma and nasopharyngeal carcinoma, and it has been implicated in some forms of Hodgkin disease and gastric carcinoma. Human herpes virus 8 (HHV-8), also known as Kaposi sarcoma herpes virus, is related to EBV. It was first identified in the tumor DNA of a patient with Kaposi sarcoma, a rare tumor until the AIDS epidemic, when it became one of the most common causes of cancer deaths among AIDS patients. HHV-8 is also believed to play a role in Castleman disease and body cavity lymphoma. Finally, human T lymphotropic virus type 1 leads to a rare tumor, adult T-cell leukemia/lymphoma, in the Far East and the Caribbean basin, as well as to some nonneoplastic diseases.

"It used to be a job to convince people that viruses were an important part of the cancer story. There had been a lot of research, but people just didn't believe it. They won-

dered, for example, why so many people who are infected don't get cancer," says Miller. "We had to fill in the details. Now people pretty much accept the idea."

"When I arrived at Yale in 1983, people didn't think these viruses were important to cancer," DiMaio says. "At conferences the human papillomavirus was always the last talk of the meeting. Now it's taken center stage." That's partly because, of all the viruses found to play an etiologic role in human cancers, the HPV types (16 and 18) linked to cervical cancer are probably the best-understood and the ones that hold the greatest promise for vaccines to be used for prevention and treatment.

Tight corsets and HPV

Early thinking on cervical cancer and what causes it would hardly suggest such a rosy scenario. In 1842 an Italian physician in Florence observed that married women in the city were getting cervical cancer, but nuns in nearby convents weren't. Although this observation would seem to point to a link between sexual activity and cervical cancer, the physician did not make this connection. He also observed that nuns had higher rates of breast cancer, and suggested that the nuns' corsets were too tight. "Clearly they had no clue," DiMaio says, "but the observation was significant."

Beginning in 1975, the virologist Harald zur Hausen, M.D., D.Sc., figured out what had eluded the Florentine physician. Zur Hausen, who for 20 years headed the German Cancer Research Center in Heidelberg, showed that HPV, a common infection spread through skin-to-skin contact and sex, could lead to cervical cancer. He and his research team successfully isolated several genotypes of the virus, some of which they linked to genital warts and others to cervical cancer.

Today, cervical cancer is responsible for 250,000 deaths each year worldwide, according to Charles J. Lockwood, M.D., the Anita O'Keefe Young Professor of Women's Health and chair of the Department of Obstetrics, Gynecology and Reproductive Sciences. In the United States, where early



"Cervical cancer is the ideal cancer in which to demonstrate the principle of anticancer vaccines, because we know what the tumor antigens are."

Janet Brandsma

screening has greatly reduced the mortality rate due to cervical cancer, about 5,000 women a year still die of the disease.

"From a mortality standpoint, the problem in this country is largely contained, but worldwide it's a huge problem," says Lockwood. "From a financial standpoint it remains a major problem in this country. The cost of surveillance and preventive treatments is astronomical (\$200 million a year just for screening), and a woman who has multiple surgical treatments for precancerous conditions of the cervix, such as cone biopsies or loop electrocautery excision procedures, is at a higher risk of giving birth to a preterm baby."

Even though cervical cancer in this country is largely under control, women still get it, and when they do, it can be devastating. Thomas J. Rutherford, PH.D., M.D., FW '94, associate professor of obstetrics, gynecology and reproductive sciences and director of gynecological oncology, recalls a patient in her mid-30s who was pregnant. The results of a routine Pap smear were abnormal. A colposcopy revealed a very high-grade squamous cell lesion. To save his patient's life, Rutherford recommended an immediate radical hysterectomy, but that would have meant losing the baby. "The patient finally agreed," Rutherford says, "but after the surgery she said to me, 'I can't believe I gave up one of my children.' It was a difficult choice she made, but she probably would have died if she hadn't."

Another patient was a 20-year-old college student who had adenocarcinoma of the cervix, which is also caused by HPV. She underwent a cone biopsy, but the Pap smear still revealed abnormalities in her cervical cells, "We couldn't repeat the procedure, because she wanted to have children," Rutherford recalls. "We put everything on the table: This is the situation. Your best option is to have a child now." The patient took Rutherford's advice and had a baby, after which Rutherford performed a radical hysterectomy. "There she was, getting married, having a baby and then having a hysterectomy, all before she turned 21," he says. "I assure you that wasn't what she foresaw for herself."

Even when a patient isn't diagnosed with a precancerous lesion, the ordeal of getting a positive test result, going back for more tests and possibly having to have a colposcopy or a biopsy before finally getting a clean bill of health is stressful. "It's also a very expensive way to prevent cervical cancer," Brandsma says. "It's a lot of money and anxiety."

A far better approach, she and other HPV experts say, would be to vaccinate people against the disease. Researchers at Yale and elsewhere have been working on two types of vaccines with promising results. A prophylactic vaccine being developed at the National Cancer Institute and the University of Washington, among other places, would prevent infection by generating a neutralizing antibody. Brandsma, DiMaio and other researchers at Yale and elsewhere are working on a therapeutic vaccine that would generate killer T-cells that could recognize tumor cells as being foreign and destroy them. "Cervical cancer is the ideal cancer in which to demonstrate the principle of anti-cancer vaccines, because we know what the tumor antigens are. Viral E6 and E7 are the oncoproteins expressed in all lesions. They're always required," Brandsma says.

Two versions of the prophylactic vaccine have shown encouraging results in clinical trials. Both prevented persistent infection by the HPV types contained in the vaccine in 100 percent of vaccinated women and reduced cervical abnormalities by more than 90 percent. Merck & Co., the maker of one vaccine, reported in the fall of 2005 that, in a Phase III trial of more than 12,000 women, the vaccine prevented virtually 100 percent of growths that can lead to cervical cancer. The company has since announced plans to file for approval with the U.S. Food and Drug Administration before the end of the year. GlaxoSmithKline, maker of the other vaccine, reported similarly positive results with its clinical trials and plans to seek approval in Europe and other countries in 2006.

Once a vaccine is in widespread use, experts predict an immediate 44 to 70 percent reduction in abnormal Pap smears and a long-term reduction of close to 95 percent



"It used to be a job to convince people that viruses were an important part of the cancer story. There had been a lot of research, but people just didn't believe it. ... Now people pretty much accept the idea."

—George Miller

in cervical cancer rates. As promising as these numbers are, the vaccine also has limitations, chief among them being that three injections are required and the vaccine must be kept refrigerated. Especially in developing countries, where the need for a vaccine is the greatest, these obstacles have the potential to limit the vaccine's efficacy. Another limitation is that, although the vaccine prevents infection by the most common high-risk HPV types, less common high-risk HPV types are not included.

Beyond that, the vaccine raises thorny social issues. To maximize its effectiveness, it should be given to girls between the ages of 9 and 12, before they become sexually active.

Already, some religious groups have raised concerns that this will be interpreted as a license to engage in premarital sex.

"These vaccines could provide a huge public health benefit," Lockwood says. "To allow their introduction to be blocked because of some extreme ideological position is unconscionable and irrational. It would be a huge cost savings, and could save some young person from dying in her 20s or 30s."

Putting cancer genes to sleep

Vaccines are not the only approach to controlling cancers with viral origins. Using the HeLa cell line, which contains HPV DNA, researchers have figured out that the proliferation of cervical cancer cells requires the expression of the HPV oncogenes E6 and E7, which are expressed by cervical carcinoma cells. These oncogenes inactivate the cancerous cells' major tumor suppressor pathways, thereby allowing the cells to proliferate.

An effective way to combat this, scientists have learned, is to induce a biological phenomenon known as senescence, an irreversible suspended animation of the cell, which acts as an important tumor suppressor mechanism. DiMaio and his colleagues have determined that the introduction of the papillomavirus protein E2 to the cell represses E6 and E7, halts cell growth and induces senescence. So, although the tumor cells have accumulated essential mutations, they still

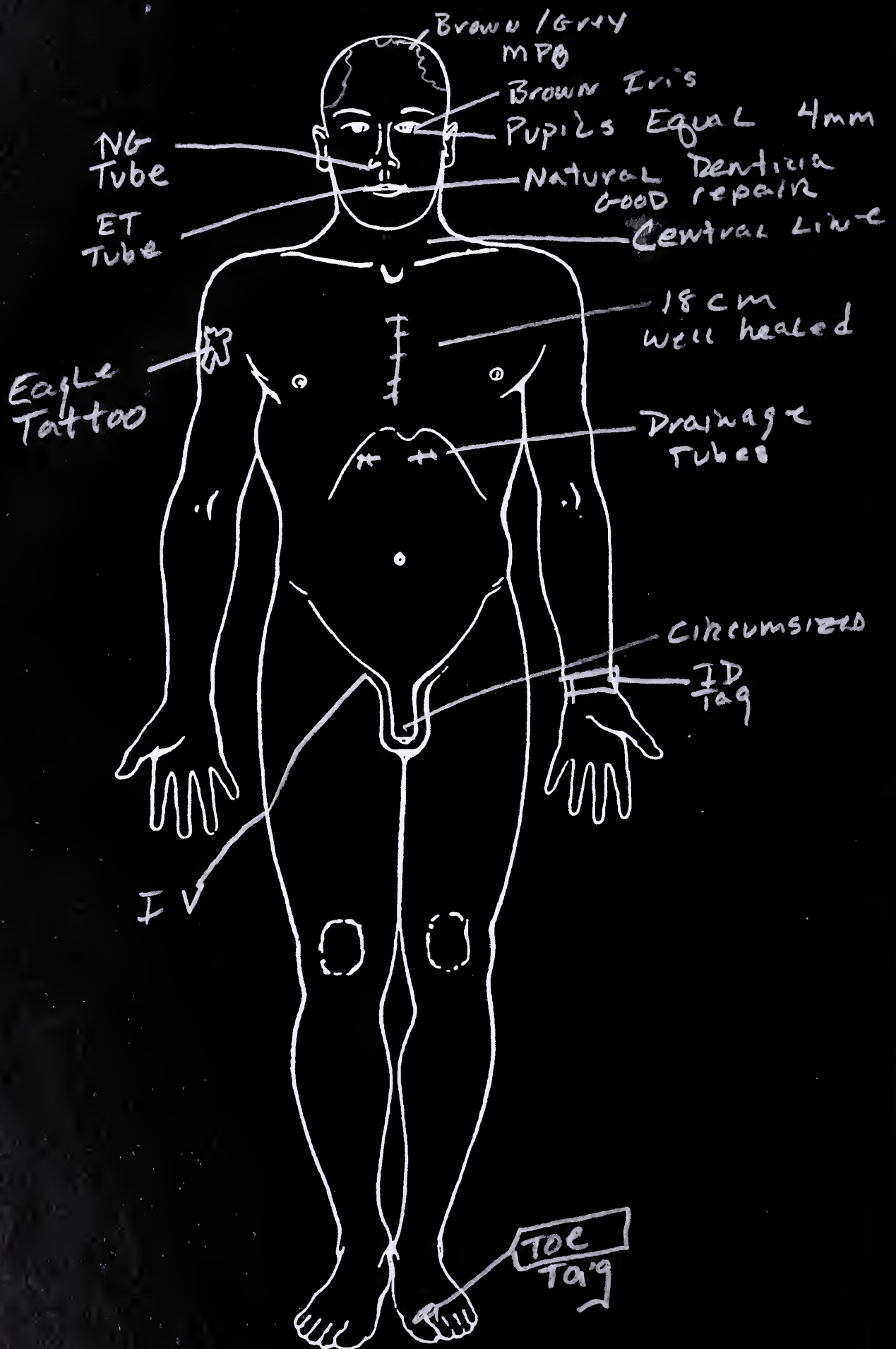
depend on the viral proteins. DiMaio likens it to a house of cards. "You need many cards to build a multistory house, but the whole edifice tumbles down if you remove the crucial card at the bottom.

"When we added E2, it induced senescence in a day or two," DiMaio says. "This creates an important barrier to tumor formation and growth. It also gives us a new model to study senescence." DiMaio says this is important because the hope is that senescence can be applied to other cancers as well. Also, there's great interest in someday inducing senescence to block aging and age-related disease. "Half of my lab is focusing on senescence," he says.

As the study of tumor virology continues to grow in importance and application, a growing number of Yale researchers are investigating other pieces of the puzzle. John K. Rose, PH.D., professor of pathology, is interested in vaccines constructed from virus vectors. He is collaborating with Brandsma's and DiMaio's labs to develop HPV vaccines using a slightly different approach. The same antigen is involved, but instead of injecting DNA into the animal, as Brandsma does, he uses virus vectors. Rose is also in charge of a small unit that has recently recruited two junior tumor virologists. Michael D. Robek, PH.D., assistant professor of pathology, studies replication of hepatitis B virus, and Robert E. Means, PH.D., assistant professor of pathology, studies ways that herpes viruses avoid the immune response.

More than 50 years ago, Henrietta Lacks was helpless against the cancer that destroyed her body, but today, thanks in part to her cells, researchers are closer than ever to defeating that enemy, and the hope is that with the knowledge gained by studying HPV, other cancer-fighting breakthroughs will soon follow.

Jennifer Kaylin is a contributing editor of Yale Medicine.



The final chapter

Once routine, autopsies are rarely performed, and pathologists lament the loss. Despite advances in medicine and laboratory science, only a post-mortem can tell the full, and final, story.

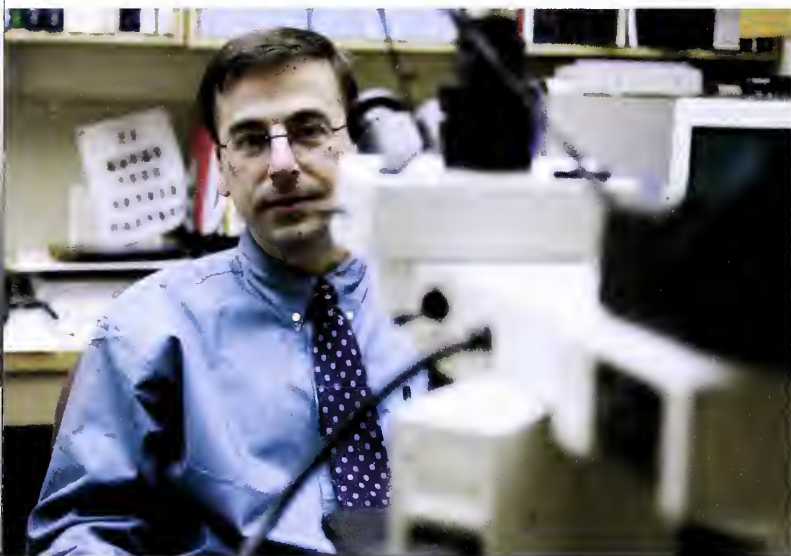
By Marc Wortman

Shortly after lunch on a midsummer's day, Charles Slater felt ill. (His name and identifying details have been altered.) Complaining of indigestion, the 55-year-old administrator at a New Haven-area social services center headed home. Soon after, though, the pain became unbearable. He called for emergency medical service and paramedics arrived within five minutes, but he had already collapsed. The paramedics could find no pulse and tried to restart his heart and breathing. In the Yale-New Haven Hospital (YNHH) Emergency Department, physicians continued efforts to restore a heartbeat, but gained no more than a slight systolic fluttering. An hour after Slater telephoned for help, the doctor in charge declared him dead.

In most respects, the end of Slater's life, although sudden and unexpected, was identical to that of all others. A biological event of catastrophic proportions overwhelmed his body. In reviewing the medical records, John H. Sinard, M.D., PH.D., HS '93, FW '94, director of the autopsy service at YNHH, says that Slater had no serious apparent health problems before that day and kept himself in decent physical shape. A heart attack seemed the likely culprit, but the body holds many secrets. His family agreed to an autopsy. In this, the end of Slater's life stands out.

While every death is ultimately the same, in the eyes of those who deal with death for a living, "each death is different," says Sinard, an associate professor of pathology

With every autopsy, Art Bellanger, manager of the autopsy service at Yale-New Haven Hospital, draws a diagram of the body, noting scars, tattoos and previous injuries.



DAPHNE GEISMAR (2)



TOP An autopsy, says John Sinard, director of the autopsy service at Yale-New Haven Hospital, “is one of the few times you consider the whole patient and the whole disease process.”

ABOVE As manager of the autopsy service, Art Bellanger performs most autopsies, with the assistance of pathology residents.

and of ophthalmology and visual science. Every time a patient dies at YNHH, the family is asked to consider an autopsy, even when the cause of death is apparent. Very few consent. About 20 percent of patients who die at YNHH are autopsied. As in most teaching hospitals, that rate is significantly above the average for private and community hospitals, which is typically below 10 percent—and half of those are required for forensic or legal reasons. (In Connecticut, forensic autopsies are performed at the Office of the Chief Medical Examiner and, in the case of crime-related deaths, are often attended by representatives from the state police.)

Pathologists at Yale worry that even the hospital’s comparatively high rate of autopsies is barely sufficient—in the 1960s, more than 70 percent of YNHH patients were autopsied at death. (The Mayo Clinic, which has one of the highest rates in the nation, autopsies more than 35 percent of patients who die in its care.) “Around the 20 percent level is the minimum to provide a reasonable statistical basis for what is seen in the hospital,” contends Raymond Yesner, M.D., a professor emeritus of pathology who, at 91, continues to serve as a research scientist in the department. “Below that level, a hospital may not be monitoring care sufficiently, and you may see problems in quality control.”

Adds Rosemarie L. Fisher, M.D., HS ’75, professor of medicine and associate dean for graduate medical education, “From an internist’s point of view, I would like to see the rate higher, although we are probably higher than a lot of other institutions. Autopsies should be performed because they often contribute to knowledge about other illnesses that may be important for the care providers or the family to know about.”

With such low rates nationally, many pathologists are concerned that medical practices may be suffering. “If you get in the range of 10 to 15 percent these days, a hospital is doing very well,” says Kim A. Collins, M.D., who chairs the autopsy committee of the College of American Pathologists, the world’s largest organization of board-certified pathologists.

“Many people think we can diagnose everything before death,” says Collins, a professor of pathology and laboratory medicine at the Medical University of South Carolina. “But studies show that in close to half the cases, autopsies find something contributory or that the whole cause of death was different than physicians believed beforehand.” With investment in health care and biomedical

research based in part on mortality statistics, the evidentiary basis for that investment may now be distorted or even false. "Without enough autopsies," Collins contends, "we really can't be accurate with our epidemiological facts."

In the age of genetic studies and imaging technologies, autopsies still provide a unique means for studying certain diseases and identifying previously unknown public health issues. Jon S. Morrow, PH.D., M.D. '76, HS '79, FW '81, the Raymond Yesner Professor of Pathology, chair of pathology and professor of molecular, cellular and developmental biology, says: "Even to this day, autopsies are essential to the identification of a number of our latest scourges, like SARS, much of AIDS and other new diseases." Moreover, he notes that even when no questions about cause of death may remain, an autopsy still provides a unique picture of a patient's health and health care, which otherwise remains incomplete. "A patient is served by many different physicians," he says. "The pathologist's evaluation is where the data come together." Those data can serve to improve teaching, research and medical care. He worries that the decline in the rate of autopsies may undermine the entire system. "We're in danger of losing a critical piece of infrastructure."

Nothing routine about death

Less than a day after Slater's death, I don a head-to-toe jumpsuit and enter the autopsy room in the morgue in an extension to the Brady Memorial Laboratory. Half a dozen people cluster around Slater's body, which lies on a long aluminum tray. Water flows continuously along a trough beneath the tray. A loud and powerful fan evacuates the air in the brightly lit room. With masks muffling our mouths and surgical caps pulled down over our ears, the echoing fan and splashing of the water make hearing difficult. Perhaps it is my own expectation, but all of us in the room seem intensely alert and attentive. There may be as many as five more autopsies performed this day, but the awesome presence of the dead and the seriousness of the investigation of death make nothing routine about any individual case.

An odor of bowels, cleansers and preservative chemicals—not quite sickening but enough to make a shower afterward a must—filters through the mask. Slater's body extends straight except for his head, which is braced by a block beneath the neck and cocked upward. A white man,

his skin is yellow, waxy and splotched with patches of purple, except for the lower third of his back, which is bruised a deep burgundy. As I soon see, his blood has pooled there. He is tall, almost as long as the table, and appears to have been in pretty good shape for his age, with little fat bunched around his waist.

He still has most of his auburn hair, which is swept back from his forehead. His brown-green eyes stare straight into the harsh overhead spotlights. His elbows, bent rigidly, hold his forearms and hands a few inches off the table, as if he died while reaching for something with both hands.

He looks alive enough that it appears he could bend his elbows and push himself off the table when Arthur J. Belanger III, M.H.S., manager of the autopsy service, approaches Slater's body and announces the present time, shortly after 1 p.m. Belanger is a jovial man with black-rim glasses and dark hair and a Navy tattoo on his thick forearm. He likes his work, enjoys explaining what he is doing and talks about it freely. With practiced swiftness, he picks up a scalpel and inserts the blade into Slater's chest just beneath the top of the left collarbone. No blood flows from the wound.

A young college student considering a future as a pathology assistant flees the room. The others—two pathology residents and an aide—watch intently. Belanger swiftly slices downward and toward the center of the chest, cutting into the rib cage. He cuts at the tip of the right collarbone and continues down until the wound intersects with the other slice. In one swift, practiced cut, he sweeps straight down the abdomen to the top of the pelvic bone. With a pair of heavy-duty snips, he snaps the last resisting bones in the rib cage and hinges open Slater's chest, exposing a sunken tangle of bluish gray, green and red organs. Belanger reaches inside Slater's body cavity. He calls out his actions as he feels with his knife to cut all the central organs free of the arteries, muscle, thorax, bone, nerves and connective tissue holding them in place.

Much to learn from the dead

Death was once the greatest biological mystery, other than life itself. No longer. Medicine and health care have progressed to the point that, when a person dies, the physiological reasons are usually apparent. In some cases, the actual time of death becomes a matter of when the switch on the life-support machinery gets turned off.

The decline in autopsy rates reflects many factors, including costs (not borne by families of patients) of up to \$3,000 per autopsy and advances in diagnostic imaging and testing methods, endoscopic exploration and surgical interventions that make cause of death all but certain in most cases. Nonetheless, "As good as those ancillary studies are, we can't diagnose everything pre-mortem," insists Collins. "Even if you know the accurate cause of death, there's still so much you can learn." According to Sinard, who serves with Collins as vice chair of the College of American Pathologists' autopsy committee, "It is one of the very few times you consider the whole patient and the whole disease process. It shows the physicians the extent of the disease process and the effectiveness of therapy for a patient. We may discover things that are entirely unexpected." For the family and the doctor, it will usually answer any outstanding questions.

Given that so much is already known about a patient's poor health and the causes of death, families often fail to grasp why an autopsy is needed at all. Many families resist what they perceive as a violation of the body after an often-arduous end of life. Perhaps as a result of all the forensic medicine series on television, many also think autopsies serve only to solve mysteries or to demonstrate a failure in their loved one's health care. They worry that the request for an autopsy indicates a problem. Yet even when it reveals no surprises, says Sinard, an autopsy can be reassuring to the family. "We're not policemen," says Morrow. "We're not looking for bad practices. We're looking for accuracy and the quality of care. An autopsy almost always substantiates that the hospital and the physician did nothing wrong."

How the news about a death is communicated can affect a family's willingness to "help" medicine. "It's the way it's presented that matters," Morrow says. "Physicians are often uncomfortable around death. They would often rather move on. The rates of autopsies, though, are higher when families are asked appropriately." Few physicians ever bother to ask; most know little about autopsies or their value and have never attended one. And few medical schools require that their students attend autopsies. At Yale, medical students attend autopsies as part of the second-year pathology course, but as with all courses in the first two years, attendance is not mandatory. "It should be a routine part of a student's education," says Collins. "Everyone needs to know about it."

Fisher, who directs Yale's residency programs, notes that residents are less likely to observe an autopsy than in years past. "There used to be a 15 percent autopsy rate required for internal medicine residency program accreditation purposes," she says. "That has just disappeared. Some programs now see only one or two autopsies a year. That's a concern."

Writing the last chapter

Even though all outward signs pointed to acute myocardial infarction—a sudden, devastating heart attack—as the cause of death, Charles Slater's family agreed to an autopsy.

With two pathology residents looking on and occasionally assisting, Belanger cuts Slater's organs—from the trachea to the testes—free of connective tissue and bone. Grasping the innards as a single mass in his arms, Belanger lifts the shiny, wet, shifting clump out of Slater's body and sets it on a large white plastic surface that covers the other leg of the L-shaped autopsy table. The pathology residents then dissect the mass of organs, paring away the connective tissue, viscera and fat. Soon, the major organs are revealed. One by one those organs and major arteries are cut free.

Belanger and an assistant turn their attention to the head. After opening Slater's skull cap with a vibrating saw, the gray brain is removed by cutting it loose from the brainstem and other soft-tissue attachments.

Meanwhile, the residents separate the removed organs, slicing the larger ones and examining the cut surfaces carefully for any signs of pathology. These are then placed on display trays for presentation to the attending pathologist. Some of the tissues, such as calcified coronary arteries, must be further prepared before they can be completely dissected.

Sinard enters the room and, with the pathology residents, reviews tissue from the organs. A resident presents the deceased's clinical story, which is then discussed in the context of the pathological findings. Sinard and the residents select tissue for further, microscopic examination. Finally, the attending and the residents will review the case and determine the most likely sequence of events that led to Slater's death. Slater, the deceased, has provided a valuable teaching tool. The residents participating in his autopsy would never otherwise have the chance to view a body's organs whole, fresh and in context. They have also

benefited from viewing the consequences of biological and medical processes.

Their inspection shows that Slater's lungs were congested with blood, a telltale sign of heart failure. The heart itself had a slight grayish discoloration in the left ventricle wall, evidence of a sudden, devastating thirst for blood. To the touch, the pinkish white coronary arteries were brittle. Although it would take later decalcification to allow them to be sliced open, that appeared to be the "smoking gun," a single factor capable of causing death. Arteriosclerosis, by far the most common cause of sudden death in middle-aged men, was clearly present.

Belanger returns the remaining viscera to Slater's body cavity and replaces the crown of his skull. His assistant sews both shut. The pathology residents remain in the room, examining the organs and helping to catalog them for preservation. They have witnessed the conclusion of a life, from within a profession that pays special respect to the patient who has died.

"I tell my residents to handle with care," says Yesner. "What you are doing is writing the last chapter in somebody's life."

The death certificate is filled out, and Slater's body is released in condition for an open-casket funeral. A veteran, he will be buried three days later with military honors in a cemetery outside New Haven.

Help for the living

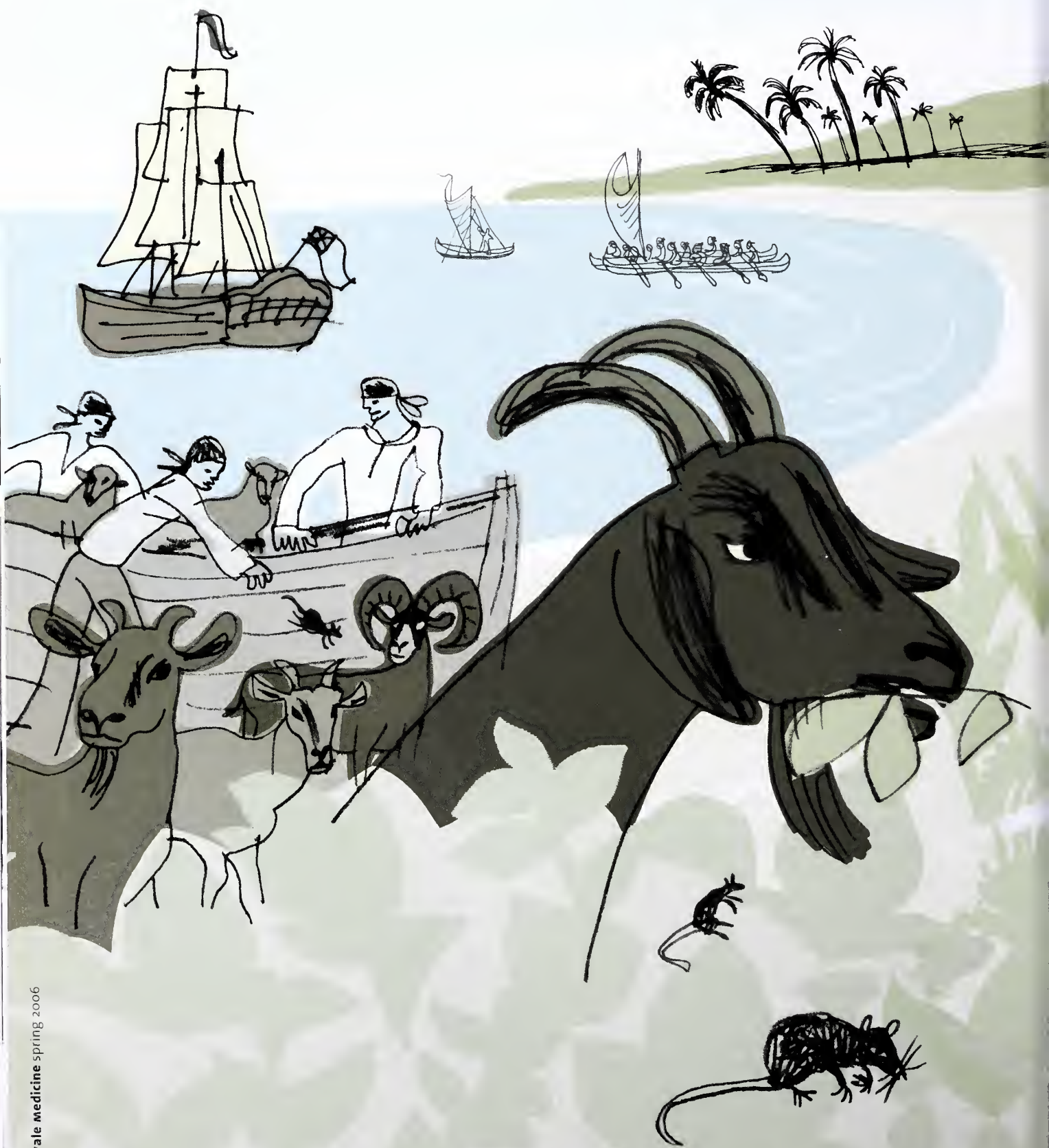
Two weeks later, the laboratory report is ready. In fact, one of the arteries had been entirely blocked by a fatty plaque that had dislodged from the artery wall, starving the heart of blood and sending it into lethal spasms as it strained for oxygen. The report also shows benign tumors developing in Slater's adrenal glands and intestine. The tumors had yet to cause symptoms, but had Slater lived, he would have encountered medical difficulties within a few years. They had not contributed to his death, but, says Sinard, "We are trying to catalog all of the disease processes in the patient." Armed with the report, his family members, who could themselves face similar conditions, will be in a position to take action. Such findings remind Collins that "there's so much you can learn about your own health by having an autopsy done on a deceased family member."

At Yale, tissue samples from every autopsy are frozen, placed in fixative solution or embedded in paraffin blocks for permanent storage. If questions should arise, tissue will be there for study—potentially avoiding exhuming a body. Longer term, the tissue may be used for teaching or research purposes. Yale possesses millions of tissue samples dating back to 1917, many of which have proven valuable for research, even decades after first being cataloged and stored. Autopsy-based research at Yale has led to a greater understanding of the worldwide flu pandemic of 1918-1919, resulted in descriptions of new forms of liver cancer and various pneumonias and expanded insights into the way blood reaches tumors. Today's research on Alzheimer's disease and other central nervous system disorders, which in most cases cannot be directly studied during a patient's lifetime, depends on autopsy material. "The speed of collecting and preserving the material is critical to the value of the specimen," says Morrow.

The national rate of autopsies has been in decline for decades. Since 1970 the Joint Commission on Accreditation of Healthcare Organizations has no longer required an autopsy rate of 20 percent to maintain accreditation. Morrow, Sinard, Collins and other autopsy pathologists have been trying to educate the medical community and the wider public about the need to reverse the trend. While there is no rate of autopsies considered minimally necessary by any national organization, "100 percent would be ideal," says Collins. "I wish we could have at least 20 percent nationally. Every family ought to be approached for the opportunity an autopsy offers them."

One day, a genetic factor may be found to underlie sudden cardiac death. Tissue collected in autopsies from patients such as Slater will almost certainly prove crucial in the development of new diagnostic methods and preventive therapies. The post-mortem picture of Slater's health may also prove directly beneficial to his own children and other relatives. "All of us will die," says Sinard. "That doesn't end what we can do for the living."

Marc Wortman is a contributing editor of *Yale Medicine*.



When animals sound a warning

Under the umbrella of a Yale center, ecologists and epidemiologists try to understand the not-always-felicitous interactions among humans, their environment and disease.

By Rhea Hirshman

Illustrations by Einat Peled

The native birds of Hawaii are vanishing. Of more than 100 species actively breeding on the islands when Capt. James Cook landed there in 1778, barely half remain and many of those are endangered. Having evolved in island isolation, with no mammalian predators, the birds were easy targets for alien rats—escapees from ships—which preyed on their eggs and their young. At the same time, bird habitats have been degraded by a range of human activities that date back more than 200 years, when cattle introduced to provide food for European settlers began to chew their way through the foliage.

But even though human activity has been damaging the Hawaiian bird population for centuries, the beginning of the population's drastic decline can be traced more precisely to 1826, when the encroachers were not bulldozers flattening delicate ecosystems or pesticides spread for agribusiness (those threats came later), but mosquitoes brought by a whaling ship from Mexico. Two weeks after the ship left, after taking on water and washing out its casks, locals were complaining to missionaries about a new kind of fly that flew at night and buzzed.

"There had been no mosquitoes in Hawaii before then," says Stephen C. Stearns, PH.D., "and these mosquitoes could transmit malaria." Not only did avian malaria decimate the



When Capt. James Cook first visited Hawaii in 1778, he brought animals previously unknown on the islands—and against which native species had no defenses. The ships that followed brought goats, cattle, sheep and mosquitoes, altering the environment in unforeseen ways.



native bird population, Stearns notes, “but when humans brought yellow fever to Hawaii, the mosquitoes were there to transmit the human disease as well.”

The interplay among human behavior, human health and disease, animal behavior and health and the ecology of the planet is the foundation of the activities of the new Center for EcoEpidemiology, which was established as part of the Yale Institute for Biospheric Studies and began operation on July 1 last year. Stearns, the Edward P. Bass Professor of Ecology and Evolutionary Biology and chair of ecology and evolutionary biology, is one of more than a dozen Yale faculty affiliated with the center. A specialist in the life history consequences of infections and disease, co-author of a widely used textbook on evolution and the founding editor of the *Journal of Evolutionary Biology*, Stearns calls the center “an important cross-disciplinary effort to both understand and anticipate the consequences of humanity’s interacting with the environment.”

Faculty from the School of Medicine (departments of Internal Medicine and Epidemiology and Public Health), the School of Forestry and Environmental Studies (FES), the Graduate School of Arts and Sciences and Yale’s Department of Ecology and Evolutionary Biology are among those participating in center activities. The center’s director, Durland Fish, PH.D., notes that—through fostering the creation of new undergraduate and graduate courses, hosting seminars and symposia, coordinating Yale’s existing cross-disciplinary curricula and helping to develop an interdisciplinary doctoral program in epidemiology and ecology/environmental science—it will be addressing two main themes.

“The first,” Fish says, “is how do we integrate environmental and ecological sciences into infectious disease epidemiology? The focus in combating diseases has traditionally been to concentrate on individual humans or discrete groups of humans—for instance, by developing diagnostic techniques or vaccines. But many important human pathogens, whether transmitted human to human, animal to human or vector to human, originate in the environment. The risks of incurring or transmitting infection have everything to do with what happens in the environment.” Fish adds, “I view infectious diseases as environmental threats—measurable and predictable. So we want to look at how to get the ecological sciences as equal participants in understanding and combating infectious diseases.”

A professor of epidemiology (microbial diseases) at the School of Public Health (EPH) and principal investigator of the Centers for Disease Control and Prevention’s Fellowship Training Program in vector-borne diseases, Fish notes that he had experienced a “lack of communication between ecology and epidemiology” throughout his career. “I studied the ecology—the abundance and distribution—of insect-borne pathogens. There wasn’t much support for this kind of work, because in the 1960s we thought we had conquered all kinds of infectious diseases with drugs and vaccines.”

However, Fish points out, diseases thought to be controlled or eliminated have re-emerged, while “new” infections including Lyme disease and West Nile virus have also surfaced. Suburbs that encroach on once-natural areas bring humans in closer contact with deer and the deer ticks that carry Lyme disease. In parts of Central and South America, a decade-long pandemic of dengue fever is attributable to an increase in the number of items such as tires and cans—used as containers or left as garbage—that hold the standing water that becomes a breeding ground for mosquitoes. In these and a wide range of other instances, zoonotic diseases—those caused by infectious agents that can be transmitted between (or are shared by) animals and humans—have everything to do with environmental disturbance, human population growth and the speed with which people, animals, plants and materials are transported around the world.

The second theme of the center, Fish says, is “getting the tools of human medical science into the hands of those studying disease ecology and environmental health.” He notes, for instance, that David K. Skelly, PH.D., another faculty member affiliated with the center, is using ultrasound technology originally developed as a diagnostic tool for humans to study parasitic cysts in frogs. Amphibians, he notes, have been central to the development of biological knowledge and have become icons for environmental decline.

“We can learn a lot about human health by looking at nonhuman systems, and the development of the field of ecoepidemiology is a recognition of that,” says Skelly, a professor of ecology at FES and of ecology and evolutionary biology, and a 2003 recipient of a Guggenheim fellowship to write a book on amphibians aimed at the general public. “Animals and plants can be sentinels—whether we’re dealing with risks that are infectious or chemical. What sorts of environmental conditions are conducive to disease? How



does the exposure of a frog in a pond to infection or toxins or pollutants translate into possible human exposure, and what are the effects of that exposure? Our message as scientists should not be only about risks to humans. But if we are modifying our environment so that reptiles are becoming hermaphrodites, we have to ask if there is a relationship to the decrease we're seeing in human male sperm counts."

While Skelly uses tools of biomedical science in his work as an ecologist, he talks in turn about the relevance of ecological tools and methods to medical research. "As an ecologist, I know that the emerging field of disease ecology shows us a discernible relationship between infectious agents and species distribution and abundance." Skelly says that the tools of ecology, including field experimentation (going out into the environment where infection happens, modifying some part of the natural world and comparing it to a control location), "are now spreading into the biomedical world—medical researchers are building models and testing them in nature, taking the study of disease outside the laboratory and looking at the environmental contexts of disease and infection."

Using Lyme disease as an example of changing perspectives on managing infection, Skelly asks, "Can we decrease Lyme disease risk by intervening with nonhuman hosts?"

Fish, who has worked on Lyme disease "since the beginning," also talks about taking a different approach. "An ecological perspective to preventing Lyme or any other vector-borne disease involves thinking about how populations are regulated by nature and how we can work within the natural environment to reduce the presence of disease vectors."

He points out that in the case of Lyme disease, reforestation of the Northeast has caused changes in the population density and distribution of the white-tailed deer and, correspondingly, its natural parasite, the deer tick. These changes have caused a Lyme disease epidemic as humans have increasingly come into contact with ticks infected with Lyme disease bacteria. "We did an experiment—using the vaccine originally developed for humans, we vaccinated mice in the woods outside of New Haven. Over the next several years, we found fewer infected ticks. While human vaccination turned out not to be an effective defense against Lyme disease, this research path is promising." The point, Fish emphasizes, "is that there is a range of options for us to work with."

From his discipline, Stearns also notes the importance of looking at "ecological context," which he describes as standard evolutionary thinking. "Every organism 'wants' to survive," he says. "We can't really understand the development of virulence or resistance or the emergence of diseases like Ebola or SARS or AIDS unless we look at that ecological context, one that humanity has often affected."

To illustrate his point, Stearns tells what he calls a cautionary medical tale—the consequences of the spread of a cattle disease (rinderpest) into Africa. Rinderpest first evolved in Eurasia, entering Africa either with General Charles Gordon's attempt to lift the siege of Khartoum in 1885 or with the Italian invasion of Ethiopia in 1895. In Africa rinderpest encountered a continent with no evolutionary experience of—or immunity to—the disease. "The rinderpest virus spread rapidly all the way south through Africa, reducing native herds of hoofed animals down to about 1 percent of their former levels," says Stearns. "Lions, whose prey were dying off, began eating people."

"In true ecological fashion," Stearns says, the effects of these events on the human population were significant. Without the grazing animals, bushes grew up along creeks and river beds—and created ideal environments for tsetse flies. "So when people tried to move back after the virus had gone through," Stearns continues, "they encountered sleeping sickness." Now, decades later, those areas that experienced a high incidence of sleeping sickness are the national parks of Africa, because giraffes and antelopes and many other wild animals are not affected by sleeping sickness, which kills both cattle and humans.

"The interactions between predators, prey, pathogens, vectors and vegetation reshaped the human ecology of a continent for a century," Stearns says. "No one could have predicted this when some sick cows came along with an invading army into northern Africa."

Looking beyond the immediate and the obvious and paying attention to the possibility of the unpredictable are central to the interdisciplinary mission of the Center for EcoEpidemiology. The overall goal is to develop an innovative curriculum among the participating schools and departments to provide training that cannot be obtained at any other American academic institution. "I'm also hoping to see more emphasis on prevention in a much more global way. We want all sorts of new ideas to emerge," says Fish, "and there is a lot of excitement about what we're doing. When the creation of the center was announced I was inundated with e-mails and phone calls from people wanting to be involved or to know more."

A listing of just some of the topics under consideration for the center's fall seminars—the impact of global warming on infectious disease, biodiversity, environmental change, wildlife as sentinels for environmental hazards, health implications of fossil fuel use, potential bioterrorism threats to the environment—illustrates the range of interests of participants and the possibilities that the center holds. Stearns envisions the center as "a place to train a new generation of graduate students to observe the world in new ways and come up with syntheses that my generation was not trained to be able to see." Skelly adds, "We want to train people who are oblivious to disciplinary boundaries. Once faculty and students from different disciplines start talking to each other, there's no telling what can happen."

For more information about the Yale Institute for Biospheric Studies Center for EcoEpidemiology, and a list of upcoming events and courses, check the center's website at <http://www.biology.yale.edu/oib/resources/yibs.htm>.

Rhea Hirshman is a freelance writer in New Haven.



Rigging the roulette wheel to slow the spread of viruses

Avian flu virus is not new. All the influenza strains that affect people have avian origins—including the virus that caused the 1918-1919 influenza pandemic, according to Durland Fish, PH.D., professor of epidemiology. That outbreak killed at least half a million people in the United States and more than 30 million worldwide. As with such other "emerging" diseases as Ebola hemorrhagic fever, Lyme disease and severe acute respiratory syndrome, or SARS, what is "new" about avian flu is a heightened awareness of the role of other species in the development of this human health hazard, says Fish. That makes it a perfect case study for the new center Fish directs, the Center for EcoEpidemiology, part of the Yale Institute for Biospheric Studies. The center's purpose is to bring together experts in ecology and epidemiology in areas where their studies intersect.

Fish highlighted one such intersection in a talk at a conference on campus last May, "Ethical Aspects of Avian Influenza Pandemic Preparedness, Part 1: Vaccines," when he discussed the necessity of focusing more resources on understanding how the virus evolves and functions in wildlife populations so that we can keep it from developing into a strain transmissible to humans.

Of the numerous strains of the influenza virus, of most concern is the H5N1 strain. "A common scenario is that avian viruses in wild-bird populations are transmitted to domestic birds or sometimes to pigs. New strains can evolve when animals are in proximity to each other," Fish says. This process is known as "recombining." Although humans have developed some

immunity to various influenza genotypes through exposure, they would be highly susceptible to the new strain were it to become widespread in the human population.

What could make that happen? Fish says that we do not know why some strains jump the species barrier to humans and others do not. "We do know," he says, "that the H5N1 strain recombined in domestic animals and is now back in the wildlife population. We saw the first human cases in the late 1990s. When several people in Southeast Asia died of a previously unknown influenza virus, the virus was studied and we now know it as H5N1."

A pandemic occurs when a virus introduced into the human population through another species moves from person to person. Rather than relying on the wholesale destruction of infected and susceptible bird populations, or pouring resources into developing a human vaccine (he notes the impracticality of vaccinating billions of people quickly), Fish suggests other ways to keep a pandemic at bay.

"The first," he says, "is to vaccinate carrier species against viral genotypes with pandemic potential by developing oral vaccines that can be distributed to wild birds through feed." Another approach would involve the introduction of a variation of the virus that produces a milder form of the infection but still maintains itself in appropriate bird populations, thus rendering the birds immune to pandemic genotypes.

Fish would like to see greater cooperation between the disciplines of ecology and epidemiology. "We should preserve wildlife, while at the same time figuring out how to keep it from being a threat. If we can buy time and learn more about the evolution of viruses in nature, we can rig the roulette wheel rather than just waiting for it to turn."

—R.H.



Making a better doctor, and better patients

After Hurricane Katrina, a day at a convention center in Texas provided lessons in dignity and sympathy.

What exactly did I think I was getting myself into? As I approached the Austin Convention Center's loading dock, which was swarming with people, it felt like an enormous hospital—a hospital not only for the sick but also for the weary-hearted. I had come simply to see whether I could help other evacuees; I didn't expect them to teach me a lesson in clinical medicine.

I had been living in New Orleans for only six days before leaving town. I never got the chance to start at Tulane's School of Public Health and Tropical Medicine. Along with my landlord and his family, I rode out Hurricane Katrina in Houma, La., a predominantly Cajun town southwest of New Orleans. I awoke the morning after the storm, surprised that I'd slept through the brunt of it. Slivers of light invaded my room through boarded-up shutters. Lawn furniture, branches, leaves and other debris lay strewn across the backyard, and the gusting wind carried an eerie chill. What next? I asked myself.

When I heard of the devastation of New Orleans, I left my refuge to stay with friends in Austin, Texas. I volunteered to help at the convention center, which housed 4,000 evacuees: some riding the high of a miraculous escape, others succumbing to depression after seeing their homes and livelihoods swept away. All, however, were emotionally fragile.

I discovered their vulnerability while distributing toiletries and clothing to people lined up for showers. Grown women reluctantly asked me for clean underwear. They'd make a request, and I would search for the right size. Sometimes I had to turn back for a larger size, embarrassing the woman I was serving. One woman asked me for a feminine hygiene product and I wasn't sure what she needed. I felt flustered and she told me to forget the request. As she walked away I knew I'd seriously messed up.

I did better when my job was to help elderly and disabled men at the showers. As I wheeled one man into the changing room, he recounted the story of a treacherous week. Together we peeled off his clothing one piece at a time: His legs wobbled as he hovered above the wheelchair. His soiled underwear dropped to his ankles, and I tossed the garment in the trash heap. Steam from the showers and the mid-day Texas sun cooked the air inside the shower room; the smell was nauseating. I had to fight the urge to rush outside for a breath of fresh air. The man's eyes showed me his underlying feelings of humiliation. I knew that registering my revulsion would only make him feel worse. So I held back my feelings and told him how wonderful his shower would feel, hot water hitting his back for the first time in 10 days. Ahh.

It doesn't take much to make a patient feel afraid or ashamed. Sometimes a reflexive shudder will do it. Or maybe a grimace or an unthinking remark. The consequences are serious. Once people are made to feel inferior or disgusting, they shut down. They're not as likely to be open, honest or compliant.

I often thought about Austin after finding a home for the fall at the Yale School of Public Health. I began using my experiences there as a lens for understanding my classes. In the health policy course, for instance, Mark J. Schlesinger, PH.D., professor of public health, explained how stigma can compromise the quality of health care. Patients with a stigmatized illness, he explained, are less likely to seek care. Furthermore, he told us, physicians are more likely to sidestep critical issues related to conditions that carry a stigma. My mind reeled back to the Austin Convention Center and I understood that when I embarrassed the woman who needed sanitary products, I had unintentionally denied her appropriate care. Later, my ability to overcome my discomfort with the man in the shower allowed me to help him without compromising his dignity.

I didn't work in a hospital, help out in an ER or scrub for surgery, but in Austin I learned something about clinical medicine. I have promised myself that when I become a physician, I will remember the lessons the evacuees taught me about the importance of unabashed sympathy. I think those lessons will make me a better doctor and help my patients to be better patients.

David Grew, of West Hartford, Conn., returned to New Orleans this spring to complete his public health studies after spending the fall semester at Yale. He hopes to enter medical school in August.

WE WELCOME SUBMISSIONS

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Pietro De Camilli Stephen Strittmatter



Ira Mellman

New center to focus on neuroscience and brain disorders

The School of Medicine has launched a new interdepartmental program, Cellular Neuroscience, Neurodegeneration and Repair (CNNR), to be led by PIETRO DE CAMILLI, M.D., FW '79, the Eugene Higgins Professor of Cell Biology, and STEPHEN M. STRITTMATTER, M.D., PH.D., the Vincent Coates Professor of Neurology and professor of neurobiology.

The CNNR will build on Yale's tradition of excellence in the neurosciences through the departments of neurobiology, molecular and cellular physiology, pharmacology, cell biology, psychiatry, neurosurgery, neurology and others, and the Child Study Center. Its goal is to foster cutting-edge basic research in cellular and molecular neuroscience, promote research on neurodegeneration and repair, translate scientific insights into therapeutic strategies to prevent or delay neuronal loss, and facilitate neural repair and restoration of function. This interdisciplinary program could have a significant impact on diseases such as Alzheimer's and Parkinson's, amyotrophic lateral sclerosis and multiple sclerosis, as well as diseases related to *polyglutamine expansion*, such as Huntington's.

De Camilli's pioneering work on synaptic vesicles, the intracellular packets that deliver neurotransmitters into the synapse, could advance the understanding of brain function, as well as the causes of Alzheimer's, Parkinson's and other diseases.

Strittmatter's identification of Nogo, a protein that blocks the regeneration of axons, has opened promising avenues in the search

for therapies to repair the adult nervous system after injury, and has given new hope to those who suffer from spinal cord injuries, stroke and neurodegenerative disorders such as Alzheimer's.

De Camilli and Strittmatter, who will retain their appointments in cell biology and neurology, respectively, will recruit up to seven new scientists for the CNNR. The searches will be carried out in collaboration with colleagues in the basic-science and clinical departments who work in the neurosciences, and the new recruits will have primary appointments in existing departments. In addition, the CNNR will provide a scientific home for more than 100 neuroscientists who now work across the Yale campus, sparking greater interactions and enhancing the scientific environment.

European group elects cell biologist as foreign member

IRA MELLMAN, PH.D. '78, chair and Sterling Professor of Cell Biology, is one of three American scientists elected as foreign members of the European Molecular Biology Organization (EMBO) at its annual meeting in Warsaw, Poland, last October. EMBO membership is a lifelong honor, and scientists are elected on the basis of proven excellence in research. Among its members are some of Europe's leading researchers, including 38 Nobel laureates. EMBO was established in 1964 to create a central molecular biology laboratory and a network that would enhance interactions among European laboratories. Currently there are more than 1,200 EMBO members in Europe, and only 100 investigators outside of Europe have been named as associate members.

"It is a real honor to be one of the very few U.S. scientists to be recognized by our most distinguished European colleagues by election to EMBO membership," said Mellman. "Science is truly an international endeavor, and I certainly plan to use this connection to further scientific exchange at all levels."

Mellman uses a combination of biochemical, genetic and imaging methods to understand complex functions of cell biology. His work has revealed basic biological mechanisms that regulate immune responses, particularly how dendritic cells initiate and control all antigen-specific immune responses. Another area of his research involves cell polarity and asymmetry and the molecular mechanisms that sort, target and transport cell membrane compo-

nents to appropriate membrane locations in different types of cells.

Mellman joined the Yale faculty in 1981 after completing his undergraduate training at Oberlin College, receiving his doctorate in human genetics from Yale in 1978 and beginning his academic career at Rockefeller University. From 1997 to 2001 he served as founding director of the Combined Graduate Program in Biological and Biomedical Sciences.

Mellman, who holds a joint appointment in the Department of Immunobiology, is an affiliate member of the Ludwig Institute for Cancer Research. He was named scientific director of the Yale Comprehensive Cancer Center in 2004. He is a fellow of the American Academy of Arts and Sciences and the Leukemia & Lymphoma Society, and he has received a Swebilius Award, the President's Research Development Award (Leukemia & Lymphoma Society) and the Yale Science and Engineering Society Medal.

**Margaret Bia****Rosemarie Fisher****Nora Groce****Zeev Kain****Christopher
van Dyck****Agnès Vignery**

Margaret J. Bia, M.D., professor of medicine, received the George F. Thornton Award at the annual meeting of the Connecticut chapter of the American College of Physicians in October. The award is given annually for outstanding contributions to medical education.

Linda K. Bockenstedt, M.D., the Harold W. Jockers Associate Professor of Medicine, has been named director for professional development and equity at the medical school. In this new position Bockenstedt will be responsible for creating programs to support the academic development of all faculty members and to encourage the growth of a diverse faculty body at the school. A special focus will be on the needs of women and underrepresented minorities.

Rosemarie L. Fisher, M.D., HS '75, associate dean for graduate medical education, has won the 2006 Courage to Lead Award from the Accreditation Council for Graduate Medical Education. The award honors designated institutional officials who have demonstrated excellence in overseeing residency programs at their sponsoring institutions. Designated institutional officials are responsible for all graduate medical education programs in a teaching hospital, community hospital or other type of institution that sponsors residency programs. Fisher oversees residency programs at Yale-New Haven Hospital.

Nora E. Groce, PH.D., associate professor of public health (global health) and anthropology, chaired UNICEF's Thematic Group on Violence Against

Disabled Children, which in November issued a report that is part of a larger report on violence against children. The study is a collaborative effort by the United Nations Secretary General's Office, the World Health Organization and UNICEF and is a follow-up to a 1999 U.N. study on children and armed conflict. The new report is intended to bring the issue of violence against children to the attention of policy-makers, governments and civil society around the globe. Corrie E. Paeglow, a graduate student in the Global Health Division at the School of Public Health, served as research associate on the project.

Sharon L. Kagan, D.ED., professor (adjunct) in the Child Study Center, has become the first woman to win three of the nation's most prestigious education awards. Kagan, a leader in early childhood education, won the 2005 Harold W. McGraw Jr. Prize in Education, the 2005 James Bryant Conant Award from the Education Commission of the States and the 2004 Distinguished Service Award from the Council of Chief State School Officers.

Zeev N. Kain, M.D., M.B.A., HS '92, FW '93, professor of anesthesiology, pediatrics and child psychiatry and vice chair of anesthesiology, has been appointed to the editorial board of the *Journal*

of Pediatric Psychology, the first anesthesiologist to hold this honor. Kain, who is also a member of the editorial boards of *Anesthesiology* and *Pediatrics*, is an international expert in the area of perioperative behavioral and physiological stress.

Each year the graduating class honors its teacher of the year with the Francis Gilman Blake Award, but this year the other three classes chose their own teachers of the year. The Class of 2006 honored **Laura R. Ment, M.D.**, professor of pediatrics and neurology, and **I. George Miller, M.D.**, the John F. Enders Professor of Pediatrics and professor of epidemiology and of molecular biophysics and biochemistry. The Class of 2007 selected **Margaret J. Bia, M.D.**, professor of medicine, and the Class of 2008 named **James D. Jamieson, M.D., PH.D.**, professor of cell biology and biology, and **Shanta E. Kapadia, M.D.**, lecturer in surgery (gross anatomy).

Jennifer P. Ruger, PH.D., M.Sc., assistant professor in the Global Health Division of the Department of Epidemiology and Public Health, was awarded the 2005 Labelle Lectureship in Health Services Research, given annually by McMaster University in Ontario, Canada. The lectureship is given to a young investigator who has a background in health economics and research that spans disciplines, and who challenges existing methods or accepted ideas in the health services community. Ruger's lecture, "Health and Global Governance: What's Justice Got to Do With It?," was presented on October 19.

Christopher H. van Dyck, M.D., FW '91, associate professor of psychiatry and neurobiology and director of the Alzheimer's Research Unit at the School of Medicine, was among six honorees at the "Removing the Mask" gala celebration held in October at the Omni New Haven Hotel. The mask motif is a metaphor for the devastating loss of identity and cognition caused by Alzheimer's disease. Gov. M. Jodi Rell was the event's honorary chair.

Agnès M. Vignery, PH.D., D.D.S., associate professor of orthopaedics and rehabilitation, has been named Yale-Pfizer Global Discovery Visiting Professor for 2005. Vignery, whose research focuses on the developmental and reconstructive processes of bone, will serve as a consultant at Pfizer's Groton (Conn.) laboratories. She will conduct collaborative research while gaining practical knowledge of the drug discovery and development process through interactions with the project teams. The program, which offers a 12-week position for one Yale faculty member to consult and do research on-site at Pfizer Global Research and Development, strengthens Yale-Pfizer alliances and provides Yale faculty with new collaborations and a better understanding of the pharmaceutical industry.

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JOHN CURTIS (3)



TOP Joxel Garcia, former commissioner of health for the state of Connecticut and current deputy director of the Pan American Health Organization, was the Commencement speaker.

ABOVE Kristin Noell-Casey, Susanna Cho, Laura Desilets and Jeff Donnelly applauded speakers at the ceremony.

RIGHT Daniel Walsh received his diploma from Dean Robert Alpern.

PA grads urged to keep learning

Only through constant learning can health professionals keep up with medicine.

At their Commencement in September the 29 members of the Physician Associate Program's Class of 2005 heard words of encouragement from Joxel Garcia, M.D., M.B.A., former commissioner of public health for the state of Connecticut and current deputy director of the Pan American Health Organization.

"These are exciting times to be in the health care field," Garcia said, citing new technology and new medical discoveries. But this day, he continued, would be a benchmark in the new graduates' careers. "Anything you do from today on is going to have an impact five, 10, 20 years from now. Today is all about you and how you are going to fulfill yourself as a person. Just make sure you do what you love to do. Never compromise yourself for things that are going to be short-lived or are not going to make you happy."

His closing admonition to the graduates was to "keep learning. ... If you are not learning you won't be able to adapt yourself ... to the new realities of life."

In keeping with Garcia's advice, Robert J. Alpern, M.D., dean of the School of Medicine and Ensign Professor of Medicine, said, "Medicine is changing so fast that what you've learned will probably be completely out of date five years from now." Noting the unequalled academic achievements of the Class of 2005, he said, "People

will look to you for leadership—not just to practice health care, but to lead it."

This year's Didactic Instructor Award for dedication and excellence in the classroom went to J.G. Collins, PH.D., professor of anesthesiology and lecturer in pharmacology. David Spiro, M.D., M.P.H., assistant professor of pediatrics (emergency medicine), and John Roney, PA-C, lecturer in pediatrics, shared the Clinical Instructor's Award, given to recognize exemplary teaching at a clinical rotation site. John P. Hayslett, M.D., HS '65, professor of medicine (nephrology) and of obstetrics, gynecology and reproductive sciences, received the Jack Cole Society Award for contributions in support of the physician associate profession.

—John Curtis





JOHN CURTIS

Proposing a new paradigm as international health hits close to home

Each October, students in medicine, nursing and public health present their findings from a summer of research abroad at the Committee on International Health Symposium Poster Session and Reception. But last year Hurricane Katrina cast a shadow as Curtis L. Patton, PH.D., director of International Medical Studies and professor of epidemiology, suggested that health issues once thought to occur only in the developing world have emerged in this country.

"The United States is clearly part of the globe," Patton said. "We have all thought of ourselves as separate and distinct and immune from disasters. We should seriously consider having students who want to do international health, do international health in the United States. Problems we have had this past fall suggest that there are opportunities to do in the United States the kind of work that is truly international."

Three students made oral presentations at the symposium. Sayaka Ogata, a nursing student, described the integration of HIV/AIDS services with family planning in rural China. Public health student Vidya Angundi studied placental malaria in western Kenya. The placenta, she noted, is susceptible to the most severe form of malaria. Carolyn Graeber, a medical student, measured central corneal thickness, a gauge of intraocular pressure that is a factor for the development of glaucoma, in Puerto Rico.

—J.C.



JULIE BROWN

Still going strong—Hunger and Homelessness Auction nets \$32,000 for local groups

Thirteen years ago a second-year student asked his classmates to join him in a fund-raising activity in which he'd participated as an undergraduate at Haverford College. Now that activity, the Hunger and Homelessness Auction, has become a tradition at the medical school, growing from a one-day affair to a flurry of activities spread over several days, including a football game, a dinner and a silent auction with hundreds of offerings. This year the auction raised \$32,225 for seven organizations in New Haven.

The first auction in 1994 netted \$3,500 and had far fewer activities, recalled Jeffrey A. Meyerhardt, M.D., '97, who organized it. "The silent auction," he said, "was just two tables." Meyerhardt, now at Harvard Medical School and the Dana-Farber Cancer Institute, returned to Yale in November to relate the history of the auction. Some things don't change, he said in a subsequent interview. William B. Stewart, PH.D., associate professor of anatomy, is still auctioning off his trademark bowtie, and Frank J. Bia, M.D., M.P.H., FW '79, professor of medicine and laboratory medicine, is still called upon, as he was this year, to serve as an auctioneer. Richard Belitsky, M.D., associate professor of psychiatry, shared this year's auctioneering chores.

Items on the block included, as in past years, weekends in faculty vacation homes, meals at restaurants or faculty homes, baby-sitting services, rides in planes and on yachts, various

FAR LEFT Sayaka Ogata, a nursing student, examined how family planning workers in the Chinese province of Henan integrated HIV/AIDS services into their work.

LEFT First-year medical student Matty Vestal and his girlfriend, Sarah Hunt, looked over items up for auction.

types of lessons (language, sports, music, art) and lots and lots of food items. Perhaps the most unusual offering, with a starting price of 50 cents, came from second-year student Maggie Hatcher: "Former rugby champ will tackle you three times this year when you least expect it." Her offer netted \$50 from a bidder who preferred to remain anonymous.

—J.C.



JOHN CURTIS

Medical student receives psychiatry fellowship

Second-year medical student MALLIKA LAKSHMI MENDU has received a 2005 Jeanne Spurlock Minority Medical Student Clinical Fellowship in Child and Adolescent Psychiatry from the American Academy of Child and Adolescent Psychiatry. The fellowship provides minority medical students with opportunities to work with outstanding child and adolescent psychiatrist mentors. James F. Leckman, M.D., the Neison Harris Professor of Child Psychiatry in the Child Study Center and professor of pediatrics, will serve as her mentor.



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Sauces, sunflowers and letters home

An Air Force surgeon in Iraq talks of his soldiers, Iraqi families and his feelings about the war.

Christopher P. Coppola, M.D., HS '01, didn't get much sleep during the four months he spent as a surgeon at Balad Air Base about 40 miles north of Baghdad.

The injured would arrive without warning. For instance, soon after Coppola, an Air Force major in the 332nd Expeditionary Medical Group, arrived in January 2005, insurgents attacked a police graduation ceremony in the nearby city of Baqubah. Six surgical teams, including Coppola's, rushed to Balad's tent-and-shipping-crate hospital as one helicopter after another delivered gruesomely injured policemen.

On other days—and nights—the burned and wounded who kept Coppola from his rest were American troops, Iraqi National Guard soldiers, children caught in the cross-fire and men and women hurt in fights or accidents on the base that housed 25,000 American troops and 7,000 civilian employees of Halliburton subsidiary KBR. Frequent mortar attacks led soldiers to nickname the base "Mortaritaville," Coppola said, but many of the insurgents' decades-old shells failed to detonate. "When they did go off, they would startle me and I usually couldn't sleep for the rest of the night," he said.

Coppola did relax a bit when the violence abated. On those days, his only responsibilities were scheduled procedures—inserting stomach tubes,

cleaning wounds. But going back to his hooch to catch up on sleep provided the unwelcome opportunity to reflect on his situation. "When you're cutting off someone's leg, you just do it, because they're going to die if you don't," Coppola explained in an interview from Lackland Air Force Base near San Antonio, Texas, where he now works. "When you have nothing to do, you start thinking about it. So I couldn't sleep."

The 37-year-old Coppola used some of his restless nights to write long letters to family and friends. His wife, Meredith, has assembled them in a self-published book, *Made a Difference for That One: A Surgeon's Letters Home From Iraq*.

Coppola described in the letters how he distracted himself from missing Meredith and their three sons and from the despair he felt about the suffering surrounding him. He ran for exercise, always wearing 35 pounds of armor and a helmet, occasionally waving to shepherds just beyond the fence; planted cilantro and sunflowers in the sandbags banked against his sleeping quarters; and earned modest fame in a moustache-growing competition. To make edible such meals as "tan stuff over rice," Coppola assembled an arsenal of sauces. In March, for instance, faced with an entree of "meat chunks ... diluted with unmentionable adulterants," he saluted St. Patrick's Day by dousing it with Goodall's of Dublin Irish Steak Sauce.

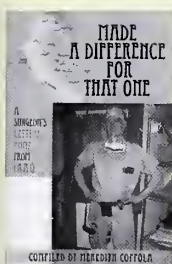
Coppola owed the Air Force six years of service in exchange for stipends while training in pediatric surgery at Children's National Medical Center and for medical school tuition at Johns

While stationed in Iraq, surgeon Christopher Coppola used an assortment of spices to liven up meals full of "unmentionable adulterants."



CHRISTOPHER COPPOLA

Hopkins. He did his general surgery residency at Yale, serving as chief resident in 2000-2001. Although he worked as an all-purpose trauma surgeon at Balad, word got around that he was a pediatric surgeon, and Iraqis brought their children to him for care: a girl with kidney failure, a boy with a prolapsed bowel. Coppola also treated children hurt in the war, including two sisters burned when their house was fire-bombed. One child recovered, but the other died. Soon after, Coppola discovered that he had unknowingly saved the life of the man who threw the bomb. "I instantly conceived of a variety of ways I could have meted justice on him with my own hands," Coppola wrote. "I've taken care of drunks who have plowed into a family of five on the highway, in the bed next to the parents whose children were



killed in the crash, but nothing prior had been as difficult as this. I was thankful I didn't know who he was while he was here."

Coppola recalled becoming injured to the carnage, only to be shocked yet again. "You feel like you've seen it all, but you haven't. There's always something worse around the corner."

Coppola opposes the war. "I want out of there, yesterday. I can't see how any father or any doctor could feel differently." And yet the work itself was rewarding. In Texas, Coppola knows that if he does not care for a patient, someone else will. In Iraq, he said, "I had the privilege of feeling that if I wasn't there, the person would probably die." And although he believes the war hurts American interests more than it helps, "If there were Americans shot at, that was the place I had to be. Trying to get those guys and women home to their families is probably the most rewarding thing I'll ever do."

Coppola expects to be sent back to Iraq this September.

—Cathy Shufro

Made a Difference for That One is sold by online booksellers and also on www.iuniverse.com. Profits go to Fisher House Foundation, which provides housing for family members of military personnel getting treatment at military medical centers.

A long, full and active life—keeping fit and taking on lots of jobs

"The trouble with retirement is that you never get a day off," is a saying quite familiar to **Henry E. Markley**, M.D. '43. At 87, Markley went into full-time retirement when Greenwich Hospital's Home Care/Hospice Program, where he worked as part-time medical director, closed in September 2004. Although he bristles at the closing of the program, which served up to 300 patients, he has no plans to slow down. An avid tennis and golf player, he continues to exercise up to an hour and a half each day, a testament to the notion that a healthy lifestyle leads to a long and healthy life.

Markley's ties to the hospital's home care program go back half a century, when an anonymous donation enabled the hospital to set up a pilot home care study for chronically ill patients who often required lengthy hospital stays. The only nursing home in Greenwich had a long waiting list, so there was a dire need for alternate long-term care. After visiting Montefiore Hospital's home care program in New York, Markley helped set up the Greenwich service, which initially accommodated only 10 patients. "By the seat of our pants we built up the program," he said. "We were a pioneer service." After a year, in 1956, the medical staff voted unanimously to request that the hospital make home care a department, and Markley continued as medical director for almost 50 years. The program was recognized across the state, serving patients from Greenwich and its surrounding communities.

Markley's medical career began with a lingering doubt. When he applied to the School of Medicine in 1939 he had little hope of being accepted. He was a top student at Penn State, but most medical schools then had an unspoken quota limiting Jews to 10 percent of any given class. One of his Jewish classmates from Penn State had already been accepted at Yale, and Markley thought it unlikely that, with a class of only 48 students, the school would accept two Jewish students from the same college. Much to his surprise, however, he entered the medical school with the Class of '43. After being drafted, he joined the Reserve so that he could postpone his Army service until he graduated. The war ended not long after he went on active service, and following an internship at Philadelphia General Hospital, he did a residency at Greenwich Hospital. He eventually received an Army assignment to Puerto Rico, which he followed up with additional training in internal medicine at Johns Hopkins. When he was offered a position on the staff at Greenwich Hospital in 1950, he returned for good to practice internal medicine.

Markley has worn many hats over the years, in addition to founding and directing the home care program. He served as the hospital's electrocardiographer for 24 years; formed the first professional medical corporation in Greenwich in 1963 with three of his fellow internists; served as chief of medical services from 1967 until 1974; and after selling his internal medicine practice in 1979, became medical director of Greenwich Health Examiners, a company that performed

In 2004 Henry Markley retired after a 60-year career in medicine, mostly at Greenwich Hospital in Connecticut. He keeps fit with tennis, golf and a healthy lifestyle.



physicals for executives. In 1993, at 75, an age when most people would have been retired, he cut back his professional activities, limiting himself to running the home care program. Although it wasn't a full-time commitment, he spent a few hours each day at the hospital reviewing charts and coordinating services.

Markley said he continued to work all these years because his father, who lived until the age of 102, retired at 75 and regretted it for the rest of his life. Even though longevity runs in his family, Markley practiced preventive medicine. He is trim, has never smoked, has only an occasional glass of wine and is very active, although age has taken a slight toll. "I'm not any good at tennis anymore," he admitted. "I know where I'm supposed to be on the court, but it takes me a while to get there."

Markley married his wife, Nicki, 13 years ago after twice becoming a widower. "The first time I was married for 25 years, the second for 20 years. I told Nicki we're not fooling around this time; we're going for 30 years," he said. Meanwhile, he has other milestones to look forward to. I went to my 60th medical school reunion," he said. "I'm looking forward to the 65th."

—Jill Max

A Montana doctor's 30 years of medicine without a safety net

On January 7, 1984, **Ron Losee, M.D.** '44, tramped out the front door of the hospital in Ennis, Mont., and into the snowy fields, intent on walking to his death. Losee, a general practitioner skilled in orthopaedic surgery, had just learned that he was being sued for malpractice by a woman who claimed that his operation on her ankle caused her undue pain during bowling. "If this was my reward by society for all my years of service, then I didn't want to live anymore. I have always tried to be the best damned doctor I could possibly be," said Losee, who since 1949 had devoted himself to his patients—even offering his own bed to patients before Ennis had a hospital. Fortunately for Losee and his loved ones, fresh bobcat tracks in the snow jolted him back to reality.

"I was fine with falling asleep in the snow and dying, but I didn't want my b***s clawed off by a bobcat," Losee said with characteristic frankness and good humor. He retraced his steps and made it home safely, although cold, cramped and tired.

In the dread-filled, six-month stretch that followed, the claim against Losee was deemed baseless; the woman's discomfort was actually caused by an injury she had sustained after Losee's surgery. However, the distaste this event left him with created the medical maverick that he is today. At the time of the lawsuit, Losee had no medical malpractice insurance. Today, at 86 vigorous years of age, Losee boasts the wherewithal and

gumption to give medical consultations, perform tennis elbow operations and practice medicine without malpractice insurance, just as he has done for the past 55 years.

Losee's decision not to carry insurance was born of practicality and the intimate nature of his practice in a rural mountain hamlet 55 miles southwest of Bozeman. He carried an insurance policy until 1975, when the cost jumped from \$8,000 to \$30,000—slightly more than his net income for the year. Losee simply could not abide passing the financial burden on to the cowboys, farmers, miners and waitresses who were already scraping together as much money as they could to pay for his services.

After the single 1984 lawsuit brought against him, Losee quite happily continued practicing medicine without malpractice insurance. But his insurance ire was rekindled by a letter he received in May 2005 from Blue Cross Blue Shield of Montana informing him that—because he does not carry malpractice insurance—he was no longer a recommended provider. The decision has had little effect on Losee, as patients still seek out his medical services. But after 55 years of sound medical practice, Losee finds it ludicrous that he is being "kicked out" of the medical system, especially since he believes that, depending on the circumstances, some doctors who commit malpractice deserve to be imprisoned. He penned a letter to Blue Cross Blue Shield sharing his strong views about the malpractice insurance industry and, as he said, "to teach them some manners." In their response, Blue Cross Blue Shield said requiring

Ron Losee dropped his malpractice insurance 30 years ago when the cost more than doubled, and he felt he could not in good conscience pass the expense along to his patients.



DUSTIN SNIPES

malpractice insurance is an industry standard designed to protect members.

In his letter, Losee detailed what he considers serious flaws in the system. "In Montana, about one-third of malpractice claims progress to lawsuits. Of these, only a small proportion end in jury trials, with physicians prevailing in the bulk of those cases," wrote Losee, who has served on the nonbinding Montana Medical Legal Panel, which comprises three doctors and three lawyers who evaluate malpractice claims to recommend whether they should proceed to trial. Malpractice insurance is, he believes, rarely needed, but the insurance industry has instilled a sense of fear in both doctors and patients to maintain the system. This fear, Losee asserted, is largely accomplished by a "bribeocracy" system of government: congressmen and senators receive large financial backing from trial lawyers and insurance-industry lobbyists to fund their reelection campaigns, while the elected officials, in return, fuel the malpractice insurance fire.

As an alternative, Losee advocates a no-fault medical liability compensation system. Instead of going to court, a malpractice claim would go to an expert panel that would assess whether an

injury has indeed been caused by a physician or other health care provider. Compensation would be doled out from a pool of money collected from tax revenues or premiums charged to doctors.

Sitting on his porch and looking out over the Madison River to the snow-capped peaks of the Rocky Mountains, Losee often reflects on his many joyful years of practice in Ennis, which began when he, his wife and their 2-year-old daughter trekked to Montana from Connecticut in 1949 in their Army Jeep. Being dropped from Blue Cross Blue Shield's provider network has certainly not slowed Losee's practice. Widely acclaimed as a physician who made major headway toward understanding and surgically repairing the "trick knee" (the Losee tests bear his name), he still sees patients and operates on tennis elbows. Patients seek Losee out and return to him time and again, based on his medical expertise and sincerity rather than the amount of malpractice insurance he carries.

—Kara A. Nyberg

The passing of two with years of service to the medical school

As the new year opened, *Yale Medicine* received word of the passing of two people with long-standing connections to the School of Medicine.

Connie Quick Tolliver, who worked for more than 30 years in the Office of Alumni Affairs at the School of Medicine, died in Hamden, Conn., on December 24 of heart failure. She was 66. Tolliver, who retired in 1995, served as assistant to the director of alumni affairs.

Henry Martone Sr. died in Daytona Beach, Fla., of complications of diabetes on December 27. He was 69. Martone was a familiar presence at the annual reunions, driving a van that shuttled alumni among various tours and dinners.

Familiar Faces

Do you have a colleague who is making a difference in medicine or public health or has followed an unusual path since leaving Yale? We'd like to hear about alumni of the School of Medicine, School of Public Health, Physician Associate Program and the medical school's doctoral, fellowship and residency programs. Drop us a line at ymm@yale.edu or write to Faces, *Yale Medicine*, P.O. Box 7612, New Haven, CT 06519-0612.



Robert Finkel



Ralph Greco



Noreen Rossi



Rock Positano and Rudolph Giuliani



Anu Gupta and Arnab Ghatak

Mary L. Warner, M.M.Sc., PA-C, assistant dean and director of the Physician Associate (PA) Program, met with PA alumni in Falmouth, Maine, in August. Joining them was Ruth Cole, widow of Jack W. Cole, M.D. '66, former chair of surgery, who founded the PA program in 1970. Attending the gathering were Frank J. Noreika, PA '94; his wife, Stacy; Lauren T. Ormsby-Pieri, PA '85; Cary J. Stratford, PA-C '80; Michelle A. Roy, PA '98; Lisa Brown, PA '04; and Sherrie A. Downing, PA-C '93.

1940s

David E. Morton, M.D. '48, HS '55, writes to say that his third granddaughter, Kan Kojima, was born last year and that he has been working on the biography of his great-grandfather, Edwin Emery. Emery, a hero on the Union side during the Civil War, was an instructor for the Revenue Cutter Service, a forerunner of the Coast Guard.

1950s

Gerard N. Burrow, M.D. '58, HS '66, has been named chair of the board of the University of Connecticut Medical Center and a trustee of the University of Connecticut. Burrow, who is president and CEO of the Mystic Aquarium & Institute for Exploration, is the David Paige Smith Professor Emeritus of Medicine and dean emeritus of the Yale University School of Medicine.

1960s

Robert I. Finkel, M.D. '65, writes to say that he retired on July 1, 2005, after 32 years of practicing

rheumatology at the Toledo Clinic. He plans to devote his energies to other interests, hobbies and, hopefully, travel.

Ralph S. Greco, M.D. '68, HS '73, the Johnson & Johnson Distinguished Professor and chief of general surgery at Stanford University School of Medicine, is one of 10 recipients of the 2006 Parker J. Palmer Courage to Teach Award, given by the Accreditation Council for Graduate Medical Education.

Karen H. Toker, M.D. '67, received the first Francis Edwards Rushton Award last year from the University of Florida Department of Pediatrics for her work in community pediatrics and child advocacy.

1970s

Robert H. Posteraro, M.D. '73, HS '78, FW '79, a radiologist with Lubbock Diagnostic Radiology in Lubbock, Texas, graduated from Oregon Health and Science University with the degree of Master of Biomedical Informatics last June.

Noreen F. Rossi, M.D. '78, professor of medicine and physiology at Wayne State University School of Medicine, has been awarded a \$1.6 million, five-year grant from the National Heart, Lung, and Blood Institute of the National Institutes of Health. She will study how regular exercise decreases blood pressure.

Alvin H. Strelnick, M.D. '75, chief of the Division of Community Health in the Department of Family and Social Medicine at Montefiore Medical Center, received the 2005 Honorary

Alumnus Award in June from the Albert Einstein College of Medicine of Yeshiva University in New York. In October he received the "Family Medicine: The Power to Change Our World" award at the northeast regional meeting of the Society of Teachers of Family Medicine.

1980s

Troyen A. Brennan, M.D. '84, J.D. '84, M.P.H. '84, professor of medicine at Harvard Medical School and professor of law and public health at the Harvard School of Public Health, has been elected to the Institute of Medicine. His research group focuses on the interwoven issues of improving patient safety and addressing the crisis in medical malpractice.

Rock G. Positano, D.P.M., M.Sc., M.P.H. '89, received a Spirit of Cabrini Award at the Cabrini Mission Foundation 2005 Gala and Awards in New York City on November 3. Also honored were NBC "Today" co-host Katie Couric and former mayor Rudolph W. Giuliani, and his wife, Judith S. Giuliani.

Positano, co-director of The Foot Center at the Hospital for Special Surgery in New York, delivered the keynote address.

1990s

Lee M. Akst, M.D. '99, was married in October to Jodi S. Wilkoff in Cleveland. Akst, who graduated from Yale College in 1995, is a fellow in laryngology at Massachusetts General Hospital. His wife is a partner in The New Teacher Project, an educational consultancy in New York.

Pauline W. Chen, M.D., HS '98, has won the Staige D. Blackford Prize for Nonfiction from the *Virginia Quarterly Review*, for her article, "Dead Enough?: The Paradox of Brain Death," published last fall.

Anu Gupta, M.D. '97, HS '00, FW '02, was married in November to Arnab Ghatak, M.D., M.B.A., in Roslyn, N.Y. Gupta directs philanthropic programs for HIV/AIDS and women's and children's health at Johnson & Johnson in New Jersey. Ghatak consults on pharmaceuticals and medical devices for McKinsey & Co.

Tim Mello, PA '99, and **Alice (Hofmann) Mello**, PA '99, announce the birth of their second child, Margaret Ella. Tim practices at Connecticut Valley Orthopedics and Sports Medicine in Springfield, Vt., and Alice practices in pediatric neurology at Dartmouth-Hitchcock Medical Center in Lebanon, N.H.

Gualberto Ruaño, Ph.D. '92, M.D. '97, president and CEO of the biomedical company Genomas, received the BEACON Medical Technology Award in September in recognition of his contributions to personalized medicine. BEACON (Biomedical Engineering Alliance and Consortium) is the professional association of the medical device industry in Connecticut.

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Remi J. Cadoret, M.D. '53, died of prostate cancer at his home in Iowa City, Iowa, on November 12. He was 77. After graduating from the School of Medicine, Cadoret spent two years in the U.S. Air Force, during which time he delivered 500 babies. He did research at the Duke University Parapsychology Laboratory in North Carolina before taking a position at the University of Manitoba College of Medicine in Canada. From there he went to Washington University in St. Louis and the University of Iowa. He was director of the Iowa Consortium for Substance Abuse and Evaluation. After his retirement in 1998 he continued his research, using adoptee studies to study gene-environment interaction, with a focus on antisocial behavior and substance dependence.

Ludmil A. Chotkowski, M.D. '42, of Berlin, Conn., died on October 6 at the age of 89. Chotkowski was an internist for more than 50 years at New Britain General Hospital, the Rocky Hill (Conn.) Veterans Home and Hospital and Connecticut Valley Hospital. He was also a self-published author, columnist, community activist, naturalist and farmer with a 14-acre fruit orchard. In Berlin, where he was born and raised on a family farm, he served as health officer, improving water quality and introducing innovative public health measures. He established one of the first clinics to administer polio vaccinations, and he performed kidney dialysis and recommended inhalers to treat asthma before these practices were widely used. In another way, however, he remained old-fashioned, continuing to make house calls.

Michael T. Cronin, D.V.M., PH.D., M.D., HS '67, assistant clinical professor of pathology, died in Branford, Conn., on November 23 of Parkinson's disease. He was 81. Cronin's medical career spanned 30 years at Yale, the Hospital of Saint Raphael and Memorial Hospital in Meriden, Conn. Early in his career, Cronin, a native of Ireland, did veterinary research at the Irish Racing Board and the Equine Research Station in England. From 1971 to 1989 he was a consulting editor for the magazine *American Scientist*.

Armin F. Funke, M.P.H. '60, died on June 24 in Roseville, Calif. He was 78. Born in Germany, Funke came to the United States in 1948 and worked at the state of California Department of Health for 30 years.

Joshua C. Gibson, M.D. '01, died on November 14 in New York of a cardiac arrhythmia. He was 34. Gibson was a fellow in infectious diseases at the Mount Sinai School of Medicine, where he co-founded the Advancing Idealism in Medicine Curriculum to help residents get involved in international programs that focus on improving the plight of others. Gibson himself worked at a refugee camp in Tanzania for Rwandan refugees, volunteered at a rural health center in India and tracked the health impact of the World Trade Center attacks on rescue workers. At a memorial service, Daniel S. Caplivski, M.D. '00, an assistant professor at Mt. Sinai, recalled his classmate, friend and colleague: "We had seen each other as first-year medical students just learning to listen through a stethoscope. Now I was watch-

ing his wonderful bedside manner and I saw his deep compassion and his meticulous attention to detail. He had become a great doctor."

James H. Greenwald, M.D. '58, died on November 14 in Chicago. He was 73. Greenwald served his internship and residency at Cook County Hospital in Chicago, then practiced nephrology and internal medicine in the Chicago area until he retired in 2000. He was a member of national medical societies and the author of several research papers.

Martha F. Leonard, M.D., a former professor of pediatrics long affiliated with the Child Study Center, died on December 27 in North Branford, Conn. She was 89. Leonard came to Yale in 1961. As an early-childhood specialist, she provided compassionate care to children and their families. She also worked to influence legislation affecting children. She was active in the Center Church in New Haven, the Interfaith Cooperative Ministries and the Community Foundation for Greater New Haven. In 1979 she received an honorary M.A.H. degree from the Yale Divinity School and later served as chaplain at the Evergreen Woods retirement community in North Branford, where she lived.

Mary Ann Lillie, R.N., M.P.H. '87, died on October 4 at the Connecticut Hospice in Branford, Conn. She was 54. Lillie worked for many years at Yale-New Haven Hospital and was an active member of St. Andrews United Methodist Church in New Haven.

Patrick J. McLaughlin Jr., M.D. '48, died on September 8 in Massachusetts at the age of 82. McLaughlin was a social worker for the city of Lowell and the Commonwealth of Massachusetts. For many years McLaughlin, who started but did not complete his medical education at Yale, and his wife lived in Andover, Mass., but recently moved to Concord to be near one of their daughters and her family.

Kay Tanaka, M.D., D.Sc., professor emeritus in the Department of Genetics, died on August 21 in New Haven. He was 76. Before coming to Yale in 1973, Tanaka held faculty positions at Baylor College of Medicine, Harvard Medical School and Massachusetts General Hospital. He founded and, from 1977 to 1989, directed the Biochemical Disease Detection Laboratory at Yale, and in 1987 he received a MERIT award from the National Institutes of Health. He was a pioneer in the use of gas-liquid chromatography and nuclear magnetic resonance in the identification of inherited metabolic diseases.

Wilbur D. Van Buren, M.D., PH.D., died on November 6 in Kansas City, Mo., of pancreatic cancer. He was 57. Van Buren began his medical studies at Yale, but obtained his degree at St. Louis University. Known as "the singing doctor," he was in private practice and worked at hospitals and nursing homes in Kansas City. He was a major in the U.S. Army Reserves, a Grand Knight of the Knights of Columbus and active in the Holy Name Catholic Church.



MICHAEL MARSLAND

A new center to fight obesity

A decade ago, when Kelly D. Brownell, PH.D., first started attracting national attention, his critics called him a “wacko,” a “food fascist” and the “grand poobah of the anti-consumer movement.” His crime? Accusing the food industry of creating a “toxic food environment” resulting in an “obesity epidemic” (See “Fighting the Good Food Fight,” Winter 2004). Three years ago he outlined the problem and proposed solutions in *Food Fight*, written with Katherine Battle Horgen, PH.D.

His goal since then has been to “change the world’s diet,” he said. “It took a long time to take the first few steps, but now things are starting to happen quickly.”

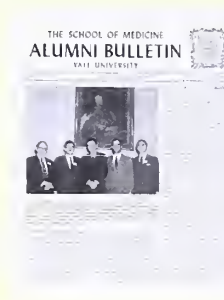
One of those advances is Yale’s new Rudd Center for Food Policy & Obesity, which Brownell, professor and chair of psychiatry and professor of epidemiology, directs. Made possible by a gift from Leslie Rudd, a vintner who hopes to affect attitudes toward food and wine in this country, the center’s goal is to improve the world’s nutrition, prevent obesity and reduce weight stigma through science-based public policy. The center opened its new offices on Edwards Street in October.

“We need to do strategic science in the interest of informing policy leaders,” said Brownell, “and we also want to make policy-makers more responsive to science.” As an example, Brownell cited the debate over soda machines in schools. “While educators may know that soft drinks aren’t especially healthy, health isn’t the main reason schools are in business. But if we can show that diet affects standardized test scores, you’d see an immediate application for public policy. That’s strategic science.”

The center’s work will involve both domestic and global initiatives, said Brownell, a reflection that the obesity crisis is worldwide. “The health minister of China recently announced that obesity and diabetes were huge problems there. The same is true in India,” he said. “You can’t understand the modern food environment without a global view. National trade policies, subsidies to the agricultural industry—all these things affect the food supply worldwide.” In addition, much obesity-related policy innovation—taxing junk food, for example—is occurring outside the United States.

“We really do want to make a difference,” said Brownell, who was named to the Institute of Medicine in October.

—Jennifer Kaylin



MAY 1956

Alumni Bulletin

The Dean’s Report

“In his annual report to the alumni of the School of Medicine on February 22, Dean Lippard reviewed the progress of the school over the past thirty-five years and outlined plans for its future development.

“Under the guidance of Drs. Blumer and Winternitz and with renewed interest of the university, the school underwent a major transformation shortly after the First World War. The faculty was reorganized, new buildings were erected, financial support was improved and enrollment increased. Graduating classes, which averaged 13 in the decade 1910-20, have increased to 80. ...

“This program [the Yale System] also requires a superior faculty, including a substantial nucleus of men who are dedicated to full-time teaching, research, and care of patients within a university hospital. ...

“The school has been successful over the years in attracting such men, and the full-time faculty now numbers about 200. Efforts have been made in recent years to strengthen clinical fields such as psychiatry, dermatology, hematology, neurology, and cardiovascular surgery, not previously represented on the full-time staff, and to broaden the range of special interests in the basic science departments. ...

“Improvement in facilities has kept pace with other developments. Most of the Medical Center has been built since 1920. The most impressive additions in the last five years are the Edward S. Harkness Memorial Hall, the Memorial Unit of the Grace-New Haven Community Hospital, and an extension of the Lauder Building for animal quarters.”



WINTER/SPRING 1981

Yale Medicine

“From This Small Sapling ...

“On December 1, shortly after noon, five men from the School of Medicine gathered in the courtyard outside the Medical Library. Some had shovels. They had come to plant a rare Oriental plane tree sapling, alleged to be a descendant of the ‘Tree of Hippocrates,’ under which the 5th-century Greek physician taught the art and science of medicine.

“The sapling was grown from seeds presented to Dr. Silver for the School of Medicine by Dr. William C. Gibson, chairman of the Universities Council of British Columbia, and a former student of Dr. John F. Fulton, the first chairman of the Department of the Hospitals of Medicine at Yale. Dr. Shope took 25 of them to his brother, William Flemer III (M.A. ’47) of the Princeton Nurseries, Kingston, N.J., who planted and nurtured them.

“Seven of the rare seeds germinated. If the one planted in the library courtyard survives the winter, the others will be planted nearby. Admittedly, the sapling is scarcely more than a twig, but historians typically are optimists. ‘The purpose of this endeavor is to establish a small park—a ‘Hippocratic Grove,’ with benches and a patio,’ said Dr. Visellear. ‘It would be a place for contemplation and study, or a pleasant spot to enjoy one’s lunch and pass the time of day.’”

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NEW BUILDINGS REFLECT COMMITMENT TO SCIENCES

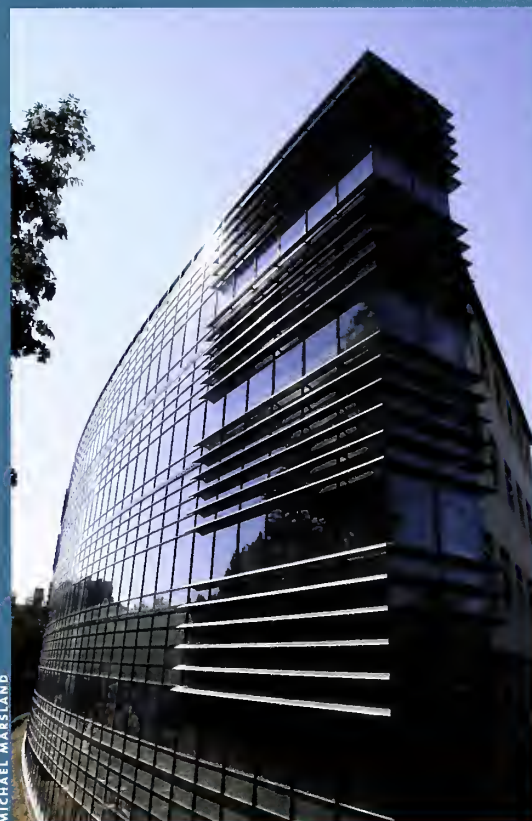
The dedication of two new buildings on the main campus in October highlighted the university's commitment to scientific research and education. The Department of Biomedical Engineering got a new home in the Daniel L. Malone Engineering Center, a five-story, 63,117-square-foot building on Prospect Street. Research there will focus on biomedical engineering, materials science and nanotechnology. The construction was made possible by a \$24 million gift from John C. Malone, a 1963 Yale College alumnus and chair of the Liberty Media Corp., and is named for his father, an engineer at General Electric.

"It stands as a statement to all that Yale engineering is an integral part of this university's most vibrant intellectual life," said Paul A. Fleury, PH.D., dean of the Faculty of Engineering. "The research and teaching that will take place here will center upon those forefront areas of biomedical engineering, materials science and nanotechnology that underpin 21st-century progress."

Also on Prospect Street is the 105,000-square-foot, three-story Class of 1954 Chemistry Research Building, the result of the largest class gift in the university's history. Each floor is dedicated to one of three areas: synthetic organic chemistry, inorganic chemistry and chemical biology. Projects under way include developing new materials for solar energy and new catalysts to facilitate hydrogen storage as a fuel source, and investigating the molecular basis for energy transduction in plant photosynthesis.

Provost Andrew D. Hamilton, PH.D., said a collaboration among the administration, the faculty and the Class of 1954 made the building possible. At the dedication Hamilton had a representative of each group help create a chemical reaction in which three clear liquids were mixed together before the solution turned to Yale blue. "It only works when all three components of the reaction are present," Hamilton said. "Cooperation is vital for continued Yale success, as this reaction continues again and again and again."

—John Curtis



The Daniel L. Malone Engineering Center is one of two new buildings on Yale's central campus that is devoted to science.

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